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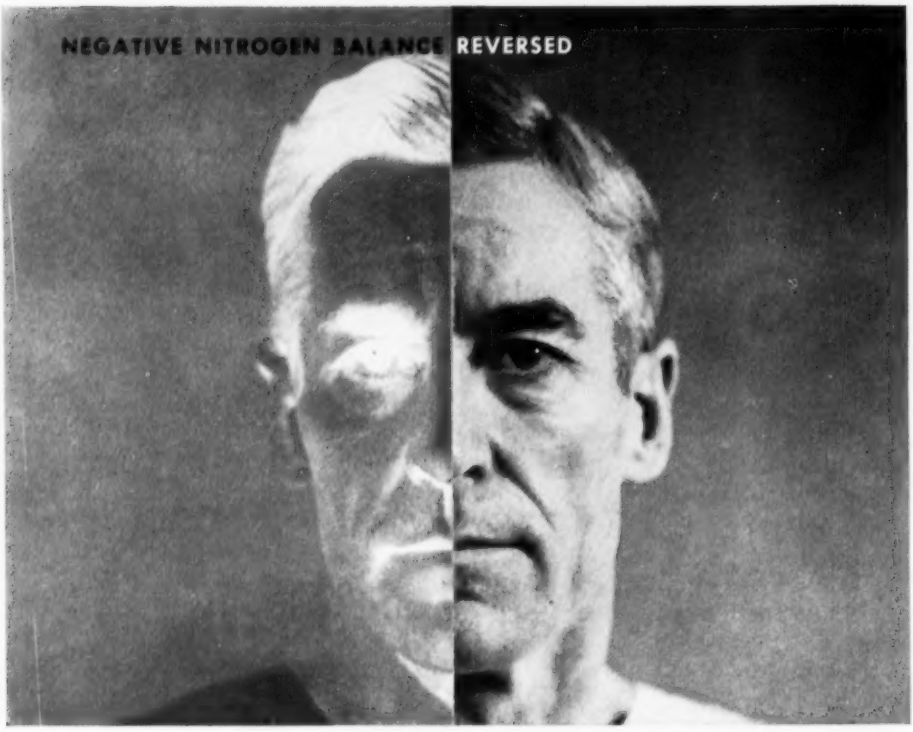

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2. Proceedings of a Conference on the Clinical Use of Anabolic Agents, Chicago, Illinois, G. D. Searle & Co., April 9, 1956, pp. 32-35.

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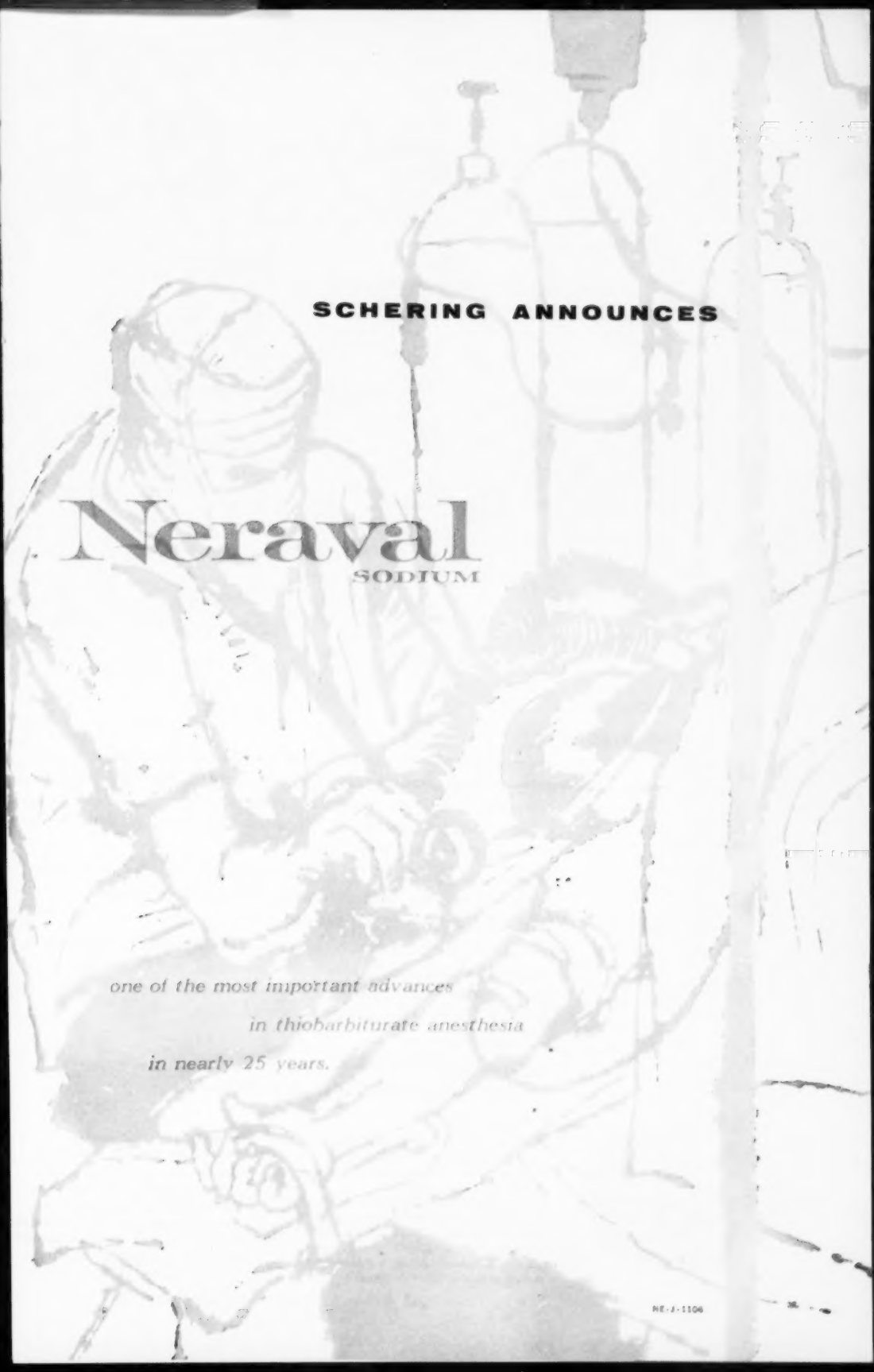
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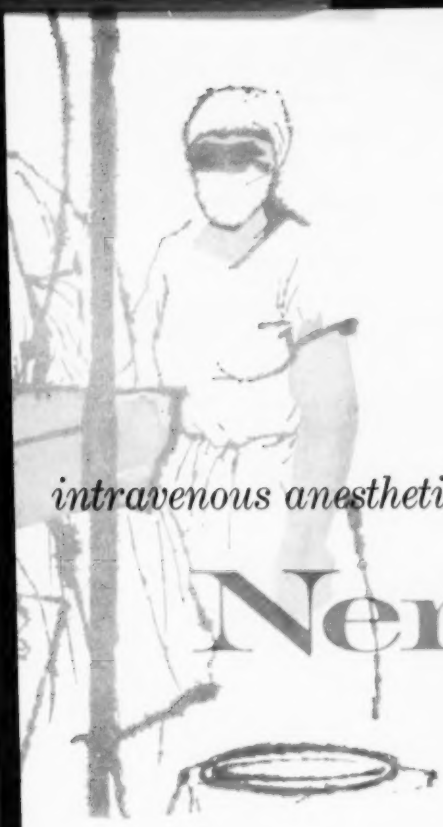

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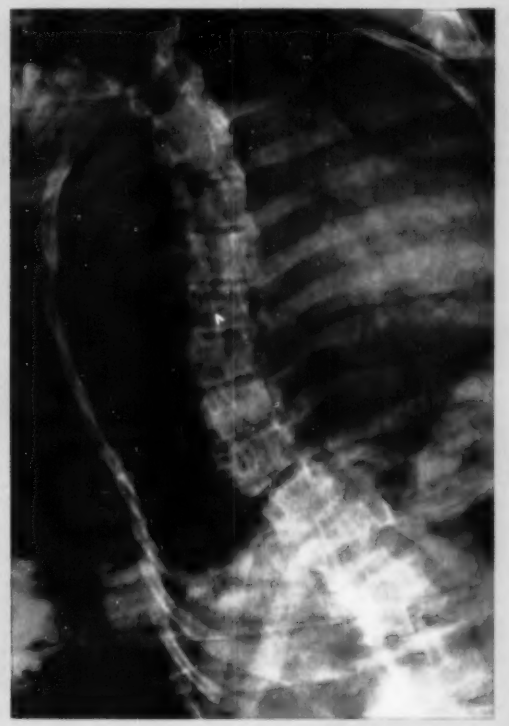

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2. Kinney, J. J.: J. M. Soc. New Jersey *53*:328 (March) 1956.
3. Weil, L. L.: Florida J. Gen. Pract. *4*:9 (July) 1954.
4. Report of Study by Army, Navy, Air Force Motion Sickness Team: J.A.M.A. *160*:755 (March 3) 1956.

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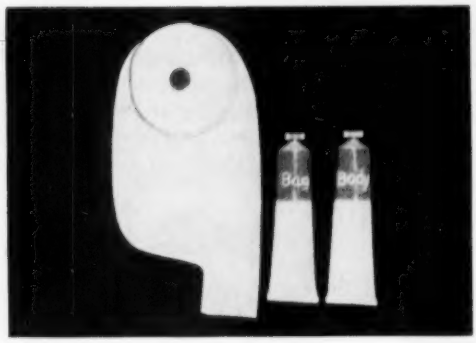

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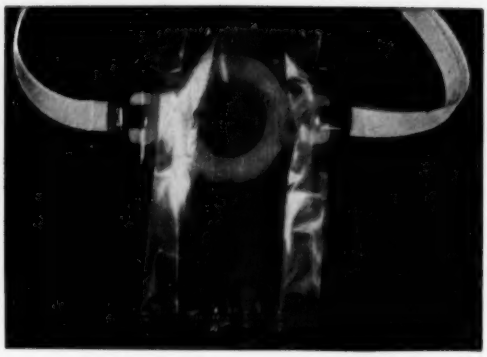

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Relationship with the Length of Normal Mucosa Excised Distal to the Lesion

ERIC P. LOFGREN, M.D.; JOHN M. WAUGH, M.D., and MALCOLM B. DOCKERTY, M.D., Rochester, Minn.

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In respect to operations for cancer of the rectum and sigmoid, local recurrences which follow the operation of combined abdominoperineal resection are diagnosed so late that little can be accomplished by reexaminations, as shown by Wangensteen and associates.[41] In the case of anterior resection, by contrast, proper use of the proctoscope in the postoperative reexamination may disclose recurrent lesions while they are still removable.

Read at the 64th Annual Meeting of the Western Surgical Association, Cincinnati, Nov. 30, 1956.

Abridgment of thesis submitted by Dr. Lofgren to the Faculty of the Graduate School of the University of Minnesota in partial fulfillment of the requirements for the degree of Master of Science in Surgery.

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But the aim of the surgeon is to prevent, rather than to treat, recurrences, and to this end he must understand the factor or factors which result in incomplete removal and subsequent regrowth of the primary tumor. How generous a margin of normal mucosa should be sacrificed proximal and distal to a malignant lesion in this region? In a review of the literature we were unable to arrive at an answer to this question based on an analysis of a controlled series. The present paper deals with such an attempt.

Definition of Terms

Anterior Resection.—This term refers to the surgical extirpation of a malignant lesion in the sigmoid colon or upper part of the rectum via the abdominal route, with end-to-end anastomosis of the bowel and with or without antecedent or concomitant performance of proximal colostomy to decompress the suture line.

Local Recurrence.—This term refers to the reappearance of malignant tissue in the proximity of the previously established anastomosis.

Anterior Resection: Historical Review

Reybard, of Lyons,[36] is credited with performing, in 1833, the first anterior resection for a cancerous growth of the sigmoid flexure. The procedure attracted the attention of other surgeons, and in the subsequent

years, with the advent of general anesthesia which facilitated intra-abdominal operations, it became standard treatment for cancers of the colon. A discouraging mortality rate of 30% to 50% was attributed by von Mikulicz[30] in 1903 to faulty anastomosis which, he said, led to fatal peritonitis. He accordingly explored the possibilities of an exteriorization technique, which had been originated previously and independently by both Bloch and Paul.[6] Von Mikulicz, employing this operation, reduced the mortality rate to 12.5%, less than a third of that accompanying primary anastomosis. The improvement in results, he said, was referable to avoidance of an intraperitoneal suture line. It was due chiefly to the work of von Mikulicz that anterior resection lost favor to the less dangerous exteriorization operation, which was further modified and improved by Rankin.[35]

Nonetheless, dissatisfaction with the exteriorization procedure persisted because it presented inherent technical difficulties when patients were obese or when they had short mesenteries. Difficulties attendant upon an uncontrolled artificial anus also were noted. Recognition of the basic principles of intestinal anastomosis resulted from the early studies by Parker and Kerr,[33] and Stone and McLanahan,[38] of the Johns Hopkins group, and this permitted reevaluation of intraperitoneal anastomosis in operations for malignant lesions of the colon. Similar reappraisal was made by Lockhart-Mummery and Drummond[25] in 1908 and by Balfour[2] in 1910, incorporating the use of a tube over which the intestine was anastomosed.

These early efforts, however, were eclipsed by the classic description in 1908 of the combined abdominoperineal approach utilized by Sir Ernest Miles.[31] Miles had been impressed by the studies of Delamare, Poirier, and Cuneo,[12] demonstrating that the lymphatic drainage of the rectum corresponds to its venous drainage, consisting of the superior, middle, and inferior routes. He thought that the perineal recurrences observed clinically are caused by metastasis into these routes, and therefore his operation was designed to extirpate all three zones of lymphatic spread. The operation of combined abdominoperineal resection thereupon gained early favor with some surgeons, but the high mortality rate which accompanied it discouraged others. It remained for Westhues,[43,44] in 1934, to point out the relative unimportance of the inferior zone of lymphatic drainage, as well as the infrequency with which a rectal malignant process metastasizes distalward.

Dixon,[13,14] impressed with the good results of the Hartman operation, reasoned correctly that, had distal metastasis been of importance in recurrence, recurrence in the rectal stump would be common. Yet he failed to find this type of recurrence, and therefore in 1930 he began to anastomose the two ends of the bowel. His subsequent studies have proved him correct, and he is credited with placing low anterior resection on a sound surgical footing.

Concern over Local Recurrence

W. J. Mayo[28] reported in 1913 a case in which local recurrence followed a Kraske operation for carcinoma of the rectum. He postulated that carcinoma cells had been disseminated by traumatic manipulation of the tumor and that these cells had implanted themselves on the raw surfaces of the tissue. This conclusion was substantiated by his observations of implants in the skin in the needle-puncture holes of another patient. Since then other reports of local recurrence after operations on the colon have been made by Gordon-Watson,[19] Thompson,[39] Gregg and Dixon,[21] Wangensteen and Toon,[42] Dunphy,[16] Gray,[20] Garlock and Ginzburg,[17] Judd and Bellegie,[24] Goligher, Dukes, and Bussey,[18] Cole and associates,[9,10,29] and Baker.[1]

Incomplete excision of the primary lesion and its satellite colonies, intramural permeation of the lesion, invisible lateral-zone spread, and retention of potentially neoplastic tissue have been listed as responsible factors.

The implantation of viable, disseminated malignant cells had been mentioned casually but not accepted as a real possibility until Goligher, Dukes, and Bussey,[18] and later Cole and associates,[9,10,29] agreed that about 50% of all local recurrences after operations for cancer of the colon very probably are caused by the implantation of viable cells in the raw tissue of the anastomosis.

Jackman,[22] in a recent unpublished series of 91 cases of anterior resection in which the patients subsequently were reexamined by proctoscope at the Mayo Clinic, found 6 with local recurrence, an incidence of 6.5%.

Factors Concerned in Local Recurrence of Carcinoma

There are five factors of importance in considering a local recurrence of carcinoma after anterior resection: (1) The primary lesion may have been incompletely excised; (2) zones of "satellite spread" may have remained, since excision must include all lymphatic and vascular avenues of escape; (3) a potential zone of malignant mucosa may have remained; (4) a new primary carcinoma may have appeared, and (5) viable, loose cancer cells may have implanted themselves.

Details concerning tangible proof of these various factors may be found by the interested reader in papers by Cole,[8] Monsarrat and Williams,[32] Black and Waugh,[5] Quer, Dahlin, and Mayo,[34] Coller, Kay, and MacIntyre,[11] Lockhart-Mummery and Dukes,[26] Seefeld and Bargen,[37] Willis,[45] Bargen, Cromar, and Dixon,[3,4] Jackman and Mayo,[23] Long,[27] Goligher, Dukes, and Bussey,[18] Cole and associates,[9,10,29] and Vink.[40] Those details which we consider of importance will be developed herein under "Results." Concerning the minimal distal margin of normal mucosa considered safe, the clearance, as expressed in 24 different reports in the literature, ranged from 1.5 to 10 cm.

Materials and Methods Used

The number of patients involved in this study was 108, plus a control group of 102. The files of the Mayo Clinic were searched for all clinical

Fig. 1.—(*a*) A 43-year-old man had a Grade *2*, Type B Dukes' lesion situated 16 cm. above the dentate line; at 31 months after removal of the primary lesion a recurrence was detected at the site of anastomosis and was successfully removed. The mucosal erosion of the Grade *2* recurrence is seen. The original removed lesion had a distal fixed clearance of 1.8 cm., and this clearance was microscopically negative. There were no adjacent polyps. (*b*) Longitudinal section across the site of anastomosis in the lesion in (*a*). It demonstrates the abrupt change from normal to malignant cells. This superficial recurrence at the site of anastomosis may be explained best by the implantation of malignant cells into the line of suture. Hematoxylin and eosin; ×6.

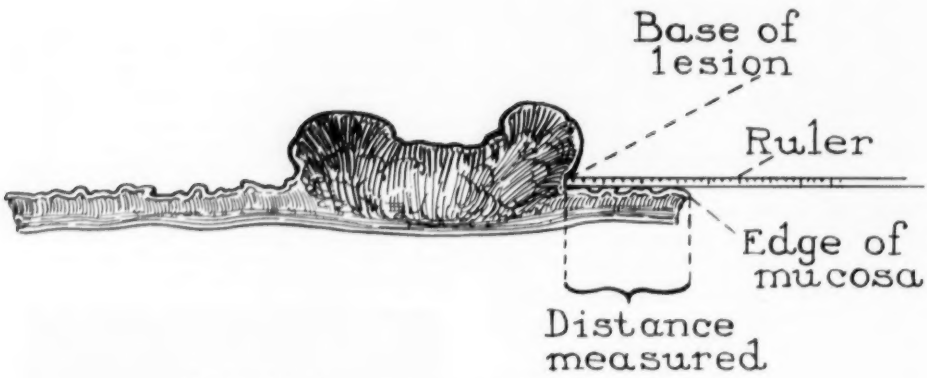
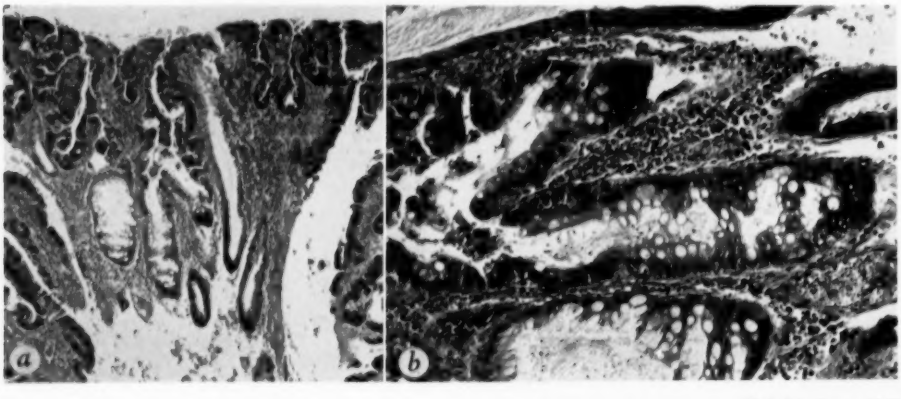


Fig. 2.—Method of measuring to the distal edge of the mucosa.

records of patients who had undergone anterior resection and in whom local recurrence had arisen. Twenty-six cases were found in which the primary operative lesions as well as removed recurrent lesions were available for study. One additional case was included; in this case all factors were identical with those in the foregoing cases except that the primary tumor had been removed by the extraperitoneal clamp technique. In 10 other cases the primary anterior resection had been carried out elsewhere, and the local recurrences had been removed at the Mayo Clinic, so that only specimens of gross recurrent lesions were available for study. The clinical records and operative specimens of 71 additional patients who had undergone anterior resection were studied. In this group of 71 patients local recurrences had developed, as proved by proctoscopic examination. Moreover, confirmation by the results of examination of tissue had been obtained in 68 cases, and by necropsy in 2 cases. In one case recurrence was considered to be present on the results of proctoscopic examination alone. These 71 local recurrences were treated by methods other than resection, usually by irradiation or fulguration or by both.

All gross specimens were formalin-fixed when studied. They consisted of 98 primary operative specimens and 37 specimens of recurrent lesions. Figure 1 illustrates the gross and microscopic appearance of a removed specimen of a recurrent lesion. A drawing was made of each specimen. In 97 of the 98 lesions (in 1 specimen the distal edge was missing), the distance (Fig. 2) from the lowermost margin of the base of the lesion to the distal edge of the mucosa at its nearest point was measured by a millimeter rule after the fixed specimen had been pressed flat. Measurements were entered on each drawing. The proximal and distal margins of the gross specimen were carefully examined for evidence of gross permeation of the lesion. Adjacent polyps were

Fig. 3.—(*a*) Transition of normal-appearing cells to malignant cells in the center crypt. Hematoxylin and eosin; reduced to 75% of mag. × 50. (*b*) Same lesion, showing the transition zone from normal to malignant-appearing mucous cells. Hematoxylin and eosin; reduced to 75% of mag. × 155.



identified and charted, but no efforts were made to locate minute polyps with the aid of a hand lens. Blocks of tissue were taken from the distal and proximal edges to ascertain the presence or absence of microscopic infiltration of the borders. A section was taken from the edge of the lesion itself for the purpose of grading. Evidence of lymphatic invasion was confirmed in the specimens known to be of Type C Dukes' classification. In the case of those reported as having no nodal involvement, a great effort was made to find all the lymph nodes for microscopic examination to rule out, as thoroughly as possible, the chance that such involvement had been responsible for the recurrence. An effort was made to secure for microscopic study tissues containing evidence of intramural spread, perineural lymphatic invasion, venous permeation, and signs of incomplete excision of the primary lesion. As mentioned previously, 98 original specimens were studied in this manner.

The 37 removed recurrent lesions likewise were studied and charted with particular reference to the site of the lesion in relation to the anastomotic line and the location of the main bulk of the lesion. Notes were made concerning whether the site of the lesion was esoenteric, intramural, or exenteric. Blocks of tissue were taken at the edge of the recurrent lesion to determine whether a transition zone from normal to malignant mucosa, as described by Long,[37] could be identified (Fig. 3*a* and *b*) and to correlate the grading of the lesion with that of the available 27 specimens of original primary lesions.

Survival data were secured from the histories and were recorded.

By way of control, the clinical records and gross specimens of another group of 102 patients known to have survived for five years after anterior resection for sigmoidal and rectal cancer were examined. The level of the lesion above the dentate line, the length of normal mucosa distal to the lesion, the grade and type of lesion, and the incidence of adjacent polyps were compared in the two groups.

Results

Of the 98 operative specimens of primary lesions studied, 47 had no evidence of metastasis to lymph nodes, and in 7 of these the lesion was confined to the wall of the bowel (Type A Dukes').[15] In 51 specimens of tissue metastatically involved lymph nodes were demonstrated. To determine what influence nodal metastasis might have had on the postoperative local recurrences, these groups were analyzed separately and were designated Groups 1 and 2, respectively.

Group 1.—Lesions in Group 1 (those without nodal metastasis) numbered 47. Thirty-three of these tumors had recurred by the 24th month, and forty had recurred by the 36th month after operation. The early recurrence in these cases suggested that retained malignant tissue was responsible. Of the 47 recurrences in Group 1, 41 were at the line of suture. In 2 of the 41 specimens malignant tissue was demonstrated at the distal sector of the transected edge, a fact which therefore represented incomplete excision of the primary lesion. In three of the original specimens perineural lymphatic involvement was demonstrated, and in one venous invasion was found, suggesting incomplete excision of the satellite spread. Two specimens exhibited multiple sentinel polyps, possibly representing zones

Fig. 4.—Multiple polyps situated adjacent to the removed cancer. These suggest that the entire mucosa was potentially neoplastic.

of potentially malignant mucosa (Fig. 4). In one of these, there were multiple small malignant polyps in the rectum 12 months after operation.

Of these 47 recurrences in Group 1, 17 had been removed, providing large specimens which could be properly oriented for study. It was found that 14 of the 17 had recurred at the line of suture. In two of these the bulk of the lesion was exenteric, with secondary mucosal erosion; in seven the lesion was evenly centered in the wall of the bowel, and in five the bulk of the lesion was intraluminal. The line of anastomosis was clearly identified in nine, but in the remaining five it had been obliterated by the carcinoma, making it necessary to base the presumed location on the proctologist's report. Two of the lesions that had recurred at the line of suture exhibited the transition zone, as described by Long,[27] and on that basis these two anastomotic recurrences were considered to be new and independent carcinomas.

Three of the recurrent tumors removed represented extra-anastomotic recurrences in that the line of suture was not involved, although the tumor was nearby. One of these was considered a new cancer, appearing 66 months after the primary operation, and exhibiting a different-grade lesion in addition to a new site free of the anastomosis. One recurrent tumor was 3 cm. proximal to the line of suture, the bulk of the lesion being intramural. The third extra-anastomotic recurrence was exenteric and adjacent to the line of suture, but not eroding into it. The second and third tumors of this group of three recurred within 16 months of the operation, and the grading of the recurrence agreed with that of the original.

Of the 30 remaining recurrences not considered amenable to removal, the proctologist stated that the recurrence was at the suture line in 27 cases and remote from the anastomosis in 3.

In summarizing the gross and microscopic analyses of the 47 original specimens in Group 1 and of the 17 removed recurrences, plus the factors of proctoscopic and biopsy verification of the other 30 recurrences, we submit the following explanations for recurrence in 15 cases. Two represented incomplete removal of the original lesion. Eight suggested incomplete excision of the local satellite spread, in which three had perineural lymphatic involvement, one had venous invasion, and four were marked by recurrence remote from the suture line, probably representing seeding at the time of operation.

These eight recurrences took place within 25 months of the original operation. Five lesions were considered new and independent, of which two exhibited the transition zone, two had potentially malignant mucosa, as evidenced by sentinel polyps, and the fifth occurred 66 months after the original operation, was situated at a new site, and had a different grading.

Group 2.—Lesions in Group 2 (those with metastasis to lymph nodes) numbered 51. It might be conjectured that metastatic processes to lymph nodes that are not removed at operation on the primary lesion account for the majority of locally recurrent lesions. It might also be reasoned that if nodal implants were the true cause of local recurrences after anterior resection, the incidence of recurrences at the site of anastomosis should be less in this group than with the lesions in Group 1. Since the lymphatic drainage extends over an area considerably wider than that confined by the suture line, it could be postulated that a lesion caused by metastasis to lymph nodes would be situated at a distance from the line of suture.

Actually, however, analysis of the data in Group 2 demonstrates that 45 of the 51 local recurrences arose at the suture line, and only 6 were located elsewhere. Thus, the proportion of lesions which recurred at the suture line in Group 2 is almost identical with that found in Group 1 (41 of 47). Of the 51 original operations in Group 2, 7 were palliative, since hepatic metastasis or exten-

sive para-aortic lymphatic spread had taken place. Of the 51 local recurrences, 39 were detected by the 24th month and 45 had occurred by the 36th postoperative month. The early reappearance of the neoplasm again suggests residual, retained malignant tissue left behind, or broken into and disseminated, at the time of the operation of the primary lesion.

Of the 45 recurrences at the line of suture, 8 had been removed and were available for study. In five most of the growth was intraluminal; in two it was intramural, and in one it was predominantly exenteric. In one original specimen of a recurrence at the suture line, malignant tissue was found at the transected edge. Of the 51 recurrent lesions, 6 were not situated at the suture line; 2 of these had been removed and were available for study.

One lesion recurred 60 months after the original operation and was detected 7 cm. distal to the suture line, where it was confined to the mucosal layer. In the original specimen, six grossly visible polyps were situated adjacent to the lesion. These events suggest that a potentially neoplastic mucosa not removed at operation was responsible for the recurrence.

The second of these two neoplasms situated at a distance from the suture line recurred 37 months postoperatively. It presented itself 6 cm. distal to the suture line and in location was predominantly exenteric. This recurrent neoplasm may have represented a true retrograde lymphatic recurrence, but it also could have resulted from seeding.

Three recurrences were distal and one was proximal to the suture line. The microscopic appearance of one of the distal recurrences, which became manifest 56 months after anterior resection, was at variance with the microscopic appearance of the original lesion; this recurrent process probably represented a new malignant lesion. The histopathologic structure of the other three lesions in this group did not exhibit such variance.

To summarize, gross and microscopic examination of the 51 original Type C Dukes'[15] specimens (Group 2) and of the 10 recurrent specimens (the latter from patients whose primary lesions had been removed elsewhere) plus the proctoscopic, biopsy, or necropsy reports on the 40 recurrences, with the addition of one clinical recurrence, provided an explanation for the local recurrence in 7 cases. One of these seven represented incomplete removal of the primary lesion; two of the seven, recurring 56 and 60 months postoperatively, respectively, were new cancers, and the remaining four, all recurring away from the suture line, are attributed to incomplete removal of the satellite spread or possibly traumatic seeding at the time of the operation on the primary lesion.

The 44 lesions which recurred at the suture line in this group of known lymphatic metastatic neoplasms could be ascribed to incomplete removal of the satellite spread if it were not for one factor: The proportion of recurrences at the suture line to the recurrences away from the suture line is almost identical in lesions of both Groups 1 and 2. This finding would not be expected on the aforementioned basis in the case of lesions in Group 2, since the area to which lymphatic metastasis of a lesion is possible is considerably more extensive than that confined by the site of anastomosis only (Group 1).

As has been said, 10 recurrent specimens were removed at the Mayo Clinic, but the primary lesions in these 10 cases, which had been removed elsewhere, were also examined. All 10 recurrences developed at the suture line. In 4 of these 10 specimens most of the tumor was exenteric; in 5 most of the neoplasm was intramural; and in 1 most of the lesion was intraluminal. In one case malignant tissue also was deposited in the abdominal scar (Fig. 5), which strongly indicates implantation. All these recurrences were detected from 11 to 59 months postoperatively.

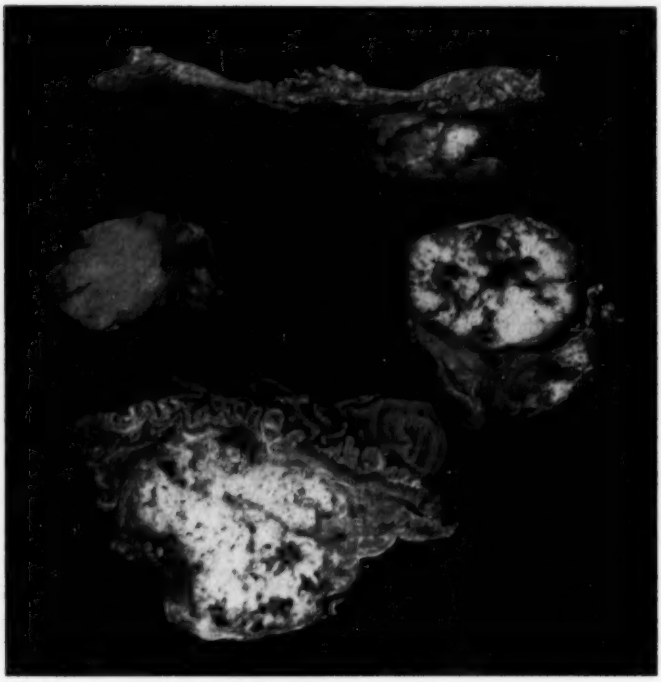


Fig. 5. — Recurrent carcinoma of the sigmoid (bottom) and metastatic implants in the abdominal scar (top) and peritoneum (right and left specimens).

Prognosis

The fate of the 108 patients in this study who had recurrent sigmoidal and rectal carcinomas should be of considerable interest and importance. Fifty-six patients underwent laparotomy; thirty-seven of them had recurrent lesions which could be removed. Those whose lesions could not be excised were treated by irradiation, or fulguration, or both. Of the 37 patients who underwent excision of recurrent lesions, 12 died within 36 months of reoperation, and 2 died in the 4th and 5th years, respectively. Of the 23 known to be living at the time of this report, only 3 had passed beyond the third postoperative anniversary. Of the 71 patients who had recurrent lesions that had irradiation or fulguration, 54 had died by the third anniversary and 7 had lived beyond three years at the time of this report. Five died in the fourth to the seventh year after the recurrence had been detected. The remainder lived only for short periods.

Of the entire group of 108 patients with recurrent cancers, 35 were living and 73 were dead at the time this was written. Of the 6 treated more than five years ago, 5 had survived, and 10 of the 17 treated prior to three years ago were living at the time of this report. Two were living at the 8th, one at the 9th, and two at the 11th year after detection and treatment. Only one of these had undergone surgical treatment of recurrence; the remainder were treated by irradiation and fulguration. Seventy-three died within five years, and the remaining twenty-nine are in a short postoperative period in which survival is "hopeful." These facts portray the grim future for a patient who has a known recurrence after anterior resection.

Patients Who Had Nonrecurrent Carcinoma

The separate group of 102 patients who had survived for five years after anterior resection were considered to have had nonrecurrent lesions and were employed as controls in evaluation of the data concerning the 108 patients with recurrent lesions. It

was found, however, that 10 of the 102 patients employed as controls had evidence of latent recurrence or metastasis from five to nine years postoperatively. Seven of these died of their original disease as late as the eighth year postoperatively, and three were living with known metastasis at the time of this report. In six additional patients new primary carcinomas developed in the esophagus, face, prostate gland, stomach, breast, and transverse colon, respectively. Thus, a five-year survival does not indicate a cure, and multiple metachronous carcinomas are a real possibility.

Correlation of Data on Recurrent Lesions, with Data on Nonrecurrent Lesions

There was no significant preponderance according to sex among patients in either group. The distribution according to age shows a slight shift toward the younger ages when recurrent lesions are considered, an observation that is in agreement with the concept that malignant disease is more virulent in the young.

When Broders' grading [7] of the recurrent lesions was compared with the grading of the nonrecurrent lesions, it was found that the distribution according to grade was almost identical. Ninety per cent of the recurrent lesions were of Grade 1 and Grade 2, whereas 93% of the nonrecurrent lesions were of the same grades. Therefore, it would appear that the degree of anaplasia has no particular significance in the incidence of local recurrence (Table 1). This is at variance with Judd and Bellegie's [24] concept that recurrence is almost predictable among lesions of high grades.

Dukes' staging,[15] which denotes a lesion confined to the wall of the bowel as Type A, a lesion that has penetrated the wall of the bowel by direct extension as Type B, and a lesion accompanied by lymphatic metastasis as Type C, also was used in the analysis (Table 1). In the group of patients with recurrent lesions 48% were free of metastasis, whereas in the group of surviving patients 64% were without metastasis.

The increase of 16% in metastasis to lymph nodes among those who had recurrent lesions suggests satellite nodal invasion as a responsible factor in local recurrence. Yet when recurrent lesions without metastasis to lymph nodes (Group 1) are compared with lesions with metastasis to lymph nodes (Group 2), the incidence of recurrences at the suture line is almost identical. If satellite nodal metastasis was a major factor in local recurrence, the incidence of recurrences at the suture line would be expected to be lower in Group 2, since the lymphatic spread extends over an area considerably wider than that demarcated by the site of anastomosis.

In the matter of the distance of the lesion from the dentate line, it was found that recurrent lesions tended to be nearer the dentate line. Eight per cent of the recurrent lesions were within 10 cm. of the dentate line, whereas only 4% of the lesions of surviving patients were within that distance. Twenty-two per cent of the recurrent lesions were situated 10 to 12 cm. above the dentate line, whereas only 6% of the lesions of surviving patients were within that distance. Twenty-nine per cent of the recurrent lesions occurred 12 to 14 cm. above the dentate line, whereas 23% of the lesions of surviving patients were within that distance. At distances more than 16 cm. from the dentate line, the percentage of occurrence was 21 for recurrent lesions and 49 for lesions of surviving patients.

TABLE 1.—*Local Recurrence of Carcinoma After Anterior Resection of the Rectum and Sigmoid* Comparison of Recurrent Lesions with Lesions of Patients Who Survived Five Years Without Recurrence, According to Dukes' and Broders' Classifications

Broders' Grading	Dukes' Classification							
	Total		A		B		C	
	R*	S	R	S	R	S	R	S
1	34	41	6	7	19	26	9	8
2	54	54	1	4	19	24	34	26
3	8	7	0	2	2	3	6	2
4	2	0	0	0	0	0	2	0
Total	98	102	7	13	40	53	51	36

*R=recurrent lesions; S=lesions of patients surviving five years without recurrences.

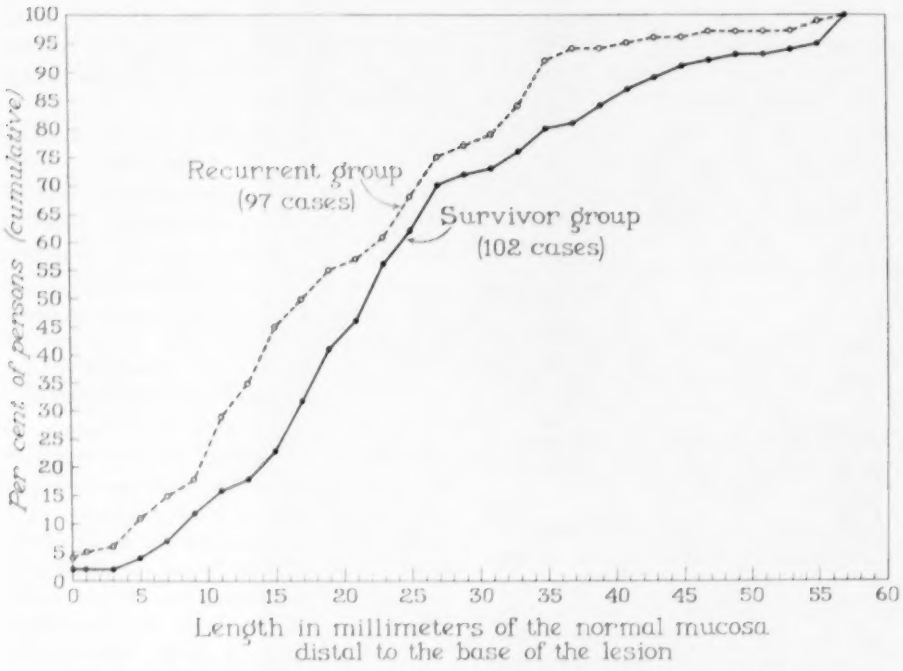


Fig. 6.—Relationship of the length of normal mucosa excised distal to the lesion among 97 patients who had recurrent carcinoma of the sigmoid and rectum and among 102 patients who survived operation for five years without recurrence. Originally there were 98 of these recurrent lesions, but 1 was omitted because the distal margin was missing from the specimen, hence, the figure of 97.

This observation is in agreement with investigations of Judd and Bellegie,[24] Garlock and Ginzburg,[17] and Wangensteen and Toon,[42] which have disclosed that the lower the situation of the intestinal lesion, the higher is the rate of recurrence and the poorer the prognosis. Why this factor applies to lesions situated more than 12 cm. above the dentate line remains obscure, for surely there is no lateral lymphatic spread of cancerous processes above this level, placed as it is well above the insertion of the levator ani muscles and above the peritoneal reflection in most cases. A factor which might be considered is the possibility that the lower the situation of the lesion, the more difficult it is to remove it, and hence the greater is the likelihood of traumatic dispersal of viable malignant cells along the raw surfaces of the operative site.

Figure 6 and Table 2 represent attempts to determine the relationship of the length of the normal mucosa excised distal to the lesion to the incidence of local recurrence. Although the incidence of recurrence is somewhat increased in the case of lesions with narrower margins, the data are not strikingly indicative of any definite trend. It therefore does not appear that a very positive relationship exists between the

TABLE 2.—*Comparison of the Length of the Distal Normal Mucosa of the Recurrent Group with the Survivors' Group*

Group	No.	0-1 Cm., %	1-2 Cm., %	2-3 Cm., %	3-4 Cm., %	4-5 Cm., %	More than 5 Cm., %
Recurrent	97	19	38	21	16	3	3
Survivors	102	12	28	31	13	9	7

TABLE 3.—*Local Recurrence of Carcinoma After Anterior Resection of the Rectum and Sigmoid*
Incidence of Polyps Adjacent to the Neoplasm as Detected at Original Gross Examination of 98 Patients Who Had Recurrent Lesions and 102 Patients Who Lived Five Years Without Recurrences

Group	No.	Polyps Present		Polyps Absent	
		No.	Per Cent	No.	Per Cent
With recurrent lesions	98	17	17.3	71	82.7
Survivors (5 yr.)	102	17	16.6	85	83.4

length of distal mucosa that is excised, as measured in formalin-fixed specimens, and the rate of recurrence. The slightly increased incidence of recurrences among lesions in which the length of normal mucosa excised was shorter perhaps may be explained on the basis of the proximity of the lesion to the operative field, increasing the density of shed viable malignant cells.[27]

It has been argued that recurrences among lower-lying lesions are the result of the tendency to cut the bowel at a site too near the lesion. This argument was not found to be valid in the present study.

If a zone of potentially malignant residual tissue was a major factor in local recurrence, the incidence of associated polyps would be expected to be higher among recurrent lesions as compared with the lesions of surviving patients (Table 3). Such a factor was not apparent in this study.

Summary and Conclusion

One hundred eight locally recurrent carcinomas which developed after the operation of anterior resection for carcinoma were studied to determine whether a relationship exists between length of normal mucosa excised distal to the original lesion and the subsequent recurrence. No strikingly significant relationship was found in a comparison of 97 of the available original specimens with the lesions from 102 patients who survived five years after anterior resection.

Other factors concerned in local recurrence of such lesions were considered. Lymphatic invasion in adjacent tissue is of importance, as evidenced by the fact that the incidence of lymphatic invasion among recurrent lesions was 16% higher than it was among nonrecurrent lesions. Yet the results of this study cast doubt on lymphatic invasion as a major factor in recurrence of malignant lesions in this location when it was demonstrated that the incidence of recurrences at the suture line was independent of the presence or absence of nodal invasion. The fact is noteworthy that in this study the situation of recurrent lesions was closer to the anus than that of lesions among surviving patients, particularly when it was found that this factor seemed to be independent of the lateral lymphatic zone.

Incomplete excision of the primary tumor explained three recurrences among the 98 original specimens. Of the 98 recurrences 12 were attributed to incomplete excision of the satellite lymphatic or vascular permeation. Potentially neoplastic mucosa, with malignant degeneration, explained seven recurrences. For the remaining 76 recurrences, all appearing at the line of suture, there was no acceptable explanation after gross and microscopic examination of 98 original excised specimens and 27 recurrent specimens from this group.

Although positive evidence that implantation of viable malignant cells into raw tissue surfaces is a major factor cannot be provided, this concept, as emphasized by Goligher, Dukes, and Bussey,[18] and later by Cole,[9] seems attractive. If valid, this concept would explain the high proportion of recurrences at the line of suture independent of the presence of nodal metastasis, the relatively early recurrence of a lesion because of residual malignant tissue after the original operation, and the cause of the slight increase in the incidence of recurrences at the lower levels above the dentate line. The concept might also explain the slight increase in recurrence of lesions when the length of

excised normal mucosa distal to the lesion was small, a factor which in itself would enhance the danger of greater traumatic shedding, with increased density, of implantable viable malignant cells at the time of the original operation. Were this hypothesis acceptable, it could apply to 77% of the local recurrences in this study.

The markedly poor prognosis for a patient after detection of a locally recurrent lesion of the type under consideration suggests that the original primary lesion had been only partially excised. Therefore, serious efforts must be exerted to avert any chance that residual malignant tissue, gross or microscopic, will remain after the first operation on the primary lesion.

Mayo Clinic.

DISCUSSION

DR. WARREN H. COLE, Chicago: I have been very interested in the dangers of the possible spread of cancer by implantation and venous emboli for the past several years, and for that reason I am particularly glad to have the opportunity to discuss this paper of Dr. Waugh and his associates. You will recall that two-thirds of his local recurrences occurred at the suture line, and he gained the impression that the most logical explanation was implantation, although, of course, he cannot prove it.

In our cases of local recurrences, we noted also that two-thirds of them occurred at the suture line; Dr. Waugh's series is much larger, and the data accordingly much more significant.

I was particularly impressed with the data of Dr. Waugh and his associates, indicating that the length of excised loop above and below the resected tumor did not appear to be related to the incidence of the local recurrences, and I agree with their impression that the extent of resection does not appear to be related to the cause of the recurrence when more than 6 cm. of bowel is resected below the tumor and 25 or 30 cm. above it.

Another reason why I believe the majority of local recurrences are not due to inadequate excision is the rarity of recurrences in a colostomy after one has done a Miles operation.

If implantation is the cause, I believe the cancer cells get there by being carried into the wall of the bowel by the suture. We are already familiar with some reports indicating that the recurrence at the suture line has taken place around a silk suture. Dr. Ackerman and Dr. McKittrick have reported such cases. There is another possibility, I suppose, of explaining this recurrence, namely, a new tumor. After the original tumor is excised, the carcinogenic agent is presumably still present; if you cut through the bowel and have a raw surface exposed, it may be that the carcinogenic agent could form a new tumor at this vulnerable point where you cut across it, namely, at the suture line. Somehow or other, I don't believe that we have enough evidence for the development of a second tumor in these circumstances to use that possibility as the explanation. I am much concerned about the possibility that we are implanting cells, and I am accordingly making a plea that we be extremely careful in our technique and try to avoid this possible cause.

We have utilized ligation of the lumen of the bowel above and below the tumor (before manipulation of the tumor) to prevent recurrence. Smears taken in the surgical pathology room indicate that outside the ligatures cancer cells are seldom demonstrable, whereas in the majority of instances smears taken inside the ligatures show cancer cells. I believe that is at least circumstantial evidence that we must be careful about the possibility of implantation.

DR. JOHN M. WAUGH, Rochester, Minn.: I would like to thank Dr. Cole for his appropriate discussion, and I would also like to emphasize that naturally we are concerned about a 6% incidence of implantation recurrence. I think, as Dr. Cole has indicated, we should take great pains to manipulate these tumors as little as possible.

However, I would point out to you that, in this series reported from the literature, Dr. Jessie Gray's recurrence rate was the highest, and yet I am sure, very gentle as she is, that from the standpoint of manipulation she likely disseminated less tumor than we less gentle males. We certainly do not feel that this would indicate that one should give up anterior resection. On the other hand, we know that the pelvic recurrence rate is high also after the combined abdominoperineal resection, and when we compare the two groups as closely as we can at the same level, with all things controlled, there is very little difference in the cure rate, so that we must break inadvertently into involved lymphatics and veins, and even in the Miles procedure must disseminate tumor to the posterior wound.

REFERENCES

1. Baker, J. W.: Responsible Resection for Carcinoma of the Rectosigmoid, editorial, West. J. Surg. 60:481-484, 1952.

2. Balfour, D. C.: Method of Anastomosis Between Sigmoid and Rectum, Ann. Surg. 51:239-241, 1910.

3. Bargen, J. A.; Cromar, C. D. L., and Dixon, C. F.: Early Carcinoma of the Colon: I. Nature and Adequate Treatment of Small Carcinomas, Arch. Surg. 43:186-191, 1941.

4. Bargen, J. A.; Cromar, C. D. L., and Dixon, C. F.: Early Carcinoma of the Colon: II. Relation Between Subclinical Inflammatory Processes and Carcinoma, Arch. Surg. 43:192-208, 1941.

5. Black, W. A., and Waugh, J. M.: Intramural Extension of Carcinoma of the Descending Colon, Sigmoid, and Rectosigmoid: A Pathologic Study, Surg. Gynec. & Obst. 87:457-464, 1948.

6. Bloch, O., and Paul, F. T., cited by Allen, A. W.: Development of Surgery for Cancer of the Colon, Ann. Surg. 134:785-796, 1951.

7. Broders, A. C.; Buie, L. A., and Laird, D. R.: Prognosis in Carcinoma of the Rectum: A Comparison of the Broders and Dukes Methods of Classification, J. A. M. A. 115:1066-1071, 1940.

8. Cole, P. P.: Intramural Spread of Rectal Carcinoma, Brit. M. J. 1:431-433, 1913.

9. Cole, W. H.: Recurrence in Carcinoma of the Colon and Proximal Rectum Following Resection for Carcinoma, A. M. A. Arch. Surg. 65: 264-270, 1952.

10. Cole, W. H.; Packard, D., and Southwick, H. W.: Carcinoma of the Colon with Special Reference to Prevention of Recurrence, J. A. M. A. 155:1549-1553, 1954.

11. Coller, F. A.; Kay, E. B., and MacIntyre, R. S.: Regional Lymphatic Metastasis of Carcinoma of the rectum, Surgery 8:294-311, 1940.

12. Delamere, G.; Poirier, P., and Cunéo, B.: The Lymphatics: General Anatomy of the Lymphatics, London, Constable & Company, Ltd., 1913.

13. Dixon, C. F.: Carcinoma of the Rectosigmoid: Resection Without Permanent Colostomy, Proc. Staff Meet. Mayo Clin. 11:384, 1936.

14. Dixon, C. F.: Anterior Resection for Malignant Lesions of Upper Part of the Rectum and Lower Part of the Sigmoid, Ann. Surg. 128: 425-442, 1948.

15. Dukes, C. E.: Classification of Cancer of the Rectum, J. Path. & Bact. 35:323-332, 1932.

16. Dunphy, J. E.: Recurrent Cancer of the Colon and Rectum: Report of Cases with Favorable Results Following Radical Surgery, New England J. Med. 237:111-113, 1947.

17. Garlock, J. H., and Ginzburg, L.: Appraisal of the Operation of Anterior Resection for Carcinoma of Rectum and Rectosigmoid, Surg. Gynec. & Obst. 90:525-534, 1950.

18. Goligher, J. C.; Dukes, C. E., and Bussey, H. J. R.: Local Recurrences After Sphincter-Saving Excisions for Carcinoma of the Rectum and Rectosigmoid, Brit. J. Surg. 39:199-211, 1951.

19. Gordon-Watson, C.: Etiology of Rectal Tumours in Relation to Treatment, Practitioner 126:481-494, 1931.

20. Gray, J.: Evaluation of Conservative Resection with End to End Anastomosis for Carcinoma of the Rectum and Lower Sigmoid Colon, Arch. Surg. 57:361-372, 1948.

21. Gregg, R. O., and Dixon, C. F.: Recurrent Carcinoma of the Colon: Report of 4 Cases, Proc. Staff Meet. Mayo Clin. 16:177-181, 1941.

22. Jackman, R. J.: Personal communication to the authors.

23. Jackman, R. J., and Mayo, C. W.: Adenoma-Carcinoma Sequence in Cancer of the Colon, Surg. Gynec. & Obst. 93:327-330, 1951.

24. Judd, E. S., Jr., and Bellegie, N. J.: Carcinoma of Rectosigmoid and Upper Part of Rectum: Recurrence Following Low Anterior Resection, A. M. A. Arch. Surg. 64:697-706, 1952.

25. Lockhart-Mummery, J. P., and Drummond, H., cited by d'Allaines, F.; Morgan, C. N., and Lloyd-Davies, O. V.: Discussion on Conservative Resection in Carcinoma of the Rectum, Proc. Roy. Soc. Med. 43:697-710, 1950.

26. Lockhart-Mummery, J. P., and Dukes, C.: Precancerous Changes in the Rectum and Colon, Surg. Gynec. & Obst. 46:591-596, 1928.

27. Long, J. W.: Recurrent Versus New Independent Carcinomas of Colon and Rectum, Thesis, Graduate School, University of Minnesota, 1949.

28. Mayo, W. J.: Grafting and Traumatic Dissemination of Carcinoma in the Course of Operations for Malignant Disease, J. A. M. A. 60:512-513, 1913.

29. McGrew, E. A.; Laws, J. F., and Cole, W. H.: Free Malignant Cells in Relation to Recurrence of Carcinoma of the Colon, J. A. M. A. 154:1251-1254, 1954.

30. von Mikulicz, J.: Small Contributions to the Surgery of the Intestinal Tract: (1) Cardiospasm and Its Treatment; (2) Peptic Ulcer of the Jejunum; (3) Operative Treatment of Severe Forms of Invagination of the Intestine, and (4) Operation of Malignant Growths of the Large Intestine, Boston M. & S. J. 148:608-611, 1903.

31. Miles, W. E.: Method of Performing Abdomino-Perineal Excision for Carcinoma of the Rectum and of the Terminal Portion of the Pelvic Colon, Lancet 2:1812-1813, 1908.

32. Monsarrat, K. W., and Williams, I. J.: Intramural Extension in Rectal Cancer, Brit. J. Surg. 1:173-182, 1914.

33. Parker, E. M., and Kerr, H. H.: Intestinal Anastomosis Without Open Incisions by Means of Basting Stitches, Bull. Johns Hopkins Hosp. 19:132-137, 1908.

34. Quer, E. A.; Dahlin, D. C., and Mayo, C. W.: Retrograde Intramural Spread of Carcinoma of the Rectum and Rectosigmoid, Surg. Gynec. & Obst. 96:24-30, 1953.

35. Rankin, F. W.; Bargen, J. A., and Buie, L. A.: Colon, Rectum and Anus, Philadelphia, W. B. Saunders Company, 1932.

36. Reybard, T. F., cited by Allen, A. W.: Development of Surgery for Cancer of the Colon, Ann. Surg. 134:785-796, 1951.

37. Seefeld, P. H., and Bargen, J. A.: Spread of Carcinoma of the Rectum: Invasion of Lymphatics, Veins, and Nerves, Ann. Surg. 118:76-90, 1943.

38. Stone, H. B., and McLanahan, S.: Resection and Immediate Aseptic Anastomosis for Carcinoma of the Colon, J. A. M. A. 120:1362-1365, 1942.

39. Thompson, J. W.: Secondary Resections in Recurring Carcinoma of the Colon, J. A. M. A. 107:1688-1692, 1936.

40. Vink, M.: Local Recurrence of Cancer in the Large Bowel: Role of Implantation Metastases and Bowel Disinfection, Brit. J. Surg. 41: 431-433, 1954.

41. Wangensteen, O. H.; Lewis, F. J.; Arhelger, S. W.; Muller, J. J., and MacLean, L. D.: Interim Report upon the "Second Look" Procedure for Cancer of the Stomach, Colon, and Rectum and for "Limited Intraperitoneal Carcinosis," Surg. Gynec. & Obst. 99:257-267, 1954.

42. Wangensteen, O. H., and Toon, R. W.: Primary Resection of the Colon and Rectum with Particular Reference to Cancer and Ulcerative Colitis, Am. J. Surg. 75:384-404, 1948.

43. Westhues, H., cited by Bacon, H. E.: Anus, Rectum, and Sigmoid Colon: Diagnosis and Treatment, Ed. 3, Philadelphia, J. B. Lippincott Company, 1949, Vol. 2.

44. Westhues, H., cited by Baker.[3]

45. Willis, R. A.: Pathology of Tumours, St. Louis, the C. V. Mosby Company, 1948.

Problems in the Diagnosis and Treatment of Gas Gangrene

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Certain current problems are contributing to critical delays in the diagnosis of gas gangrene and limitations of its treatment. As a result, this infection continues to be one of the most dreaded complications of wounds of violence with its rapid and fulminating course, profound toxemia, mutilating effects, and high mortality.

The infrequency of the occurrence of gas gangrene in civilian surgical practice has added to the difficulty. Although recent studies of the bacterial flora of accidental and war wounds have shown the presence of clostridial contamination to be 3.8% to 88.0%,[1,2] depending upon the type of wound, the incidence of clinical gas gangrene has been relatively infrequent. In a compiled series of 187,936 major open wounds,[1] the average incidence of gas gangrene was 1.76%, varying between 0.3% and 5.26%. Since surgeons are confronted with this condition so infrequently, they are often unfamiliar with the early signs and symptoms and do not anticipate its development in accidental wounds or wounds of violence.

All cases of gas gangrene seen at the Cincinnati General Hospital between 1933 and 1956 and those seen by one of us (W. A. A.) in consultation in and about Cincinnati since 1940 are currently being reviewed and analyzed. To date, a total of 42 cases have been studied. A consideration of various problems encountered in this review is undertaken here in the interest of earlier diagnosis, better treatment, and lower mortality.

Read at the 64th Annual Meeting of the Western Surgical Association, Cincinnati, Nov. 30, 1956.

From the Department of Surgery, University of Cincinnati College of Medicine, and the Cincinnati General Hospital.

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Signs and Symptoms of Developing Gas Gangrene

It must be emphasized that this disease is usually recognized by the clinical appearance of the patient and his lesion in its more obvious, far-advanced, and often irreversible stages. The presence of casts, splints, or large dressings, necessary for the treatment of the major injury, obscures the area of the wound and makes the observation and interpretation of local signs difficult and indirect. For these reasons, it is important to remove dressings promptly and to inspect the wound directly in the presence of the early symptoms of this infection. A high index of suspicion should always be held in patients with severe wounds associated with laceration or crushing of muscle.

Difficulties in recognizing gas gangrene seem to stem largely from two factors: confusion as to the nature and types of gas gangrene, and the belief that this infection is associated with the development of the usual signs of pyogenic inflammation, with extending redness of the skin, cellulitis, lymphangitis, purulent exudation, high fever, high leukocytosis, and frequent septicemia.

A useful classification of clostridial infections in our experience is as follows:

A. Clostridial myositis
   1. Spreading or diffuse (gas gangrene)
      a. Crepitant
      b. Noncrepitant or edematous
      c. Anaerobic toxemia
   2. Localized myositis
      a. Crepitant
      b. Noncrepitant

B. Clostridial cellulitis (crepitant or anaerobic cellulitis)

It is important that the surgeon realizes that clostridial myositis may be caused by one or more of a variety of these anaerobes and that the clinical picture varies with the bacterial species concerned. The most important causative micro-organism is Clostridium welchii, which was present in all but three of the 42 cases in this series, either alone or in combination with other Clostridia, which include C. novyi, C. sporogenes, and C. sordelli.

A review of our cases has emphasized the importance of the following points in the recognition of gas gangrene.

1. A variable interval existed between injury and the development of the lesion, which was as short as six hours, particularly in wounds associated with gross devitalization and contamination of muscle. The average incubation period, however, was 53 hours.

2. Pain was the earliest and most important symptom, being secondary to the rapid infiltration of the infected muscle by edema and gas. It generally persisted after primary treatment of the wound and gradually increased thereafter.

3. Rapidity and feebleness of the pulse usually followed the onset of pain and were characteristically out of all proportion to the elevation of the temperature. In advanced or progressive lesions, the changes in the pulse became increasingly apparent and progressed to circulatory collapse which was abrupt, progressive, or severe. The average pulse rate at the time of diagnosis was 118, and the extremes were 100 and 160.

4. Early, the blood pressure was normal or slightly elevated. Later, it became significantly lowered, falling precipitously in some instances to 40 mm. Hg or less.

5. Temperature elevation in the early stages of this infection varied considerably, the average being 101 F. The lowest temperature was 97, and the highest was 107. Fever was not, therefore, a reliable index of the severity and extent of the infectious progress. A low or subnormal temperature, associated with a markedly rapid pulse, was indicative of a grave prognosis. A state of severe septic shock with anuria occurred in 5 of the 42 patients.

6. The general appearance of the patient was also of some significance early in the course of the disease. Usually, he developed a peculiar grayish pallor, weakness, and profuse sweating. The usual malar flush associated with pyogenic infections was replaced by a striking pallor.

7. The mental state was often one of apathy and indifference, the patient being conscious and usually unaware of the seriousness of his condition. Stupor, delirium, prostration, and coma were late symptoms of an overwhelming infection.

Fig. 1.—Photograph of an area of early clostridial myositis (gas gangrene) which developed within 14 hours as a complication of a compound fracture—dislocation of both bones of the forearm at the wrist. Note swelling of forearm and tense, shiny skin. Serial roentgenograms showing the spread of gas in the tissues facilitated the diagnosis which was proved by operation. Highly virulent Clostridium welchii bacteria were isolated from the wound discharge.

Fig. 2.—Far-advanced case of clostridial myositis in a 17-year-old patient with compound fracture of the tibia and fibula. The discoloration of the skin, large vesicles, and irreversible gangrenous changes are obvious. Open high-thigh amputation was necessary.

8. Gastrointestinal symptoms were usually not marked, anorexia being a fairly constant finding, but vomiting was uncommon.

9. The appearance of the local lesion was not that of a pyogenic inflammation. Early, the overlying skin was either white, shiny, and tense or essentially normal in appearance (Fig. 1). An irritating dirty, brownish, watery discharge with a peculiar foul odor usually escaped from the wound. As the swelling increased, the overlying skin became dusky and bronze or khaki color in appearance. In far-advanced cases further discoloration occurred, and vesicles filled with dark-red fluid appeared on the cutaneous surface and later coalesced (Fig. 2). The changes in the color of the skin appeared earlier in the more superficial and confined types than in the deep and highly invasive types. Crepitation was palpable in 38 of the 42 cases as a relatively late sign. The underlying muscle was usually discolored, edematous, and nonviable. It frequently herniated through a fasciotomy incision (Fig. 3). The temperature of the extremity distal to the infected wound was reduced, and the skin was cold to the touch in advanced lesions.

Microscopic examination of the watery discharge revealed numerous red blood cells and many large Gram-positive bacteria with squared ends but without spores. In contrast to pyogenic infections, few pus cells were seen.

10. Laboratory examinations were helpful. In many instances a marked reduction in the number of red blood cells or of the hematocrit or hemoglobin values occurred. The leukocyte count usually was not elevated above 12,000 to 15,000. The lowest was 8800, and the highest was 57,000, the average being 21,000. The average CO_2-combining power was 30 vol. %.

Bacteriological Diagnosis of Gas Gangrene.—There are no satisfactory laboratory

Fig. 3.—Far-advanced gas gangrene of the leg, which developed about a compound comminuted fracture of the tibia and fibula. The cast has just been removed. Note vesicles filled with dark fluid, gangrenous patches of skin, and marked swelling with herniation of discolored edematous muscle through fasciotomy incision.

tests for the early diagnosis of gas gangrene, and it must be kept in mind that valuable time may be lost in awaiting results of various diagnostic tests. Rapid spread of the infection occurs within periods of two to four hours, and irreversible changes develop in the tissues rapidly. For this reason it has become more practical for us to explore surgically and without delay any wound in which the presence of clostridial myositis is suspected. This plan permits early and radical incision with decompression of the fascial compartments or excision of infected, devitalized bundles of muscle before amputation becomes necessary.

However, valuable information usually can be obtained from the microscopic examination of exudate prepared by Gram staining. The various Clostridia present are usually quite large, present squared ends, and rarely show sporulation. A method of rapidly identifying C. welchii, the most important and commonest cause of gas gangrene, was developed in our laboratory.[3] It consists of the inoculation of infectious exudate into special milk media which are then incubated anaerobically four to five hours. The development of typical stormy fermentation in the milk media and the demonstration that the proliferating bacteria are motile are indicative of the presence of C. welchii.

Inability to Differentiate Between True Toxigenic Infection Produced by Clostridia in Wounds and Secondary Nontoxigenic Action in Mixed Infections.—The demonstration of this organism in wounds by bacteriological methods often suggests that incipient or early gas gangrene is present. In addition, Clostridia are demonstrated in many active infections of wounds with or without crepitation. Experience has shown that the presence of crepitation often is the result of other nonclostridial organisms, such as Escherichia coli and Aerobacter aerogenes. One of the renal problems that exists in the diagnosis of early gas gangrene at this time is our inability to determine whether Clostridia found in an area of infection are actually contributing to the development of that infection and its associated toxemia.

Fig. 4.—Roentgenogram of elbow and arm, showing presence of an increasing amount of gas in the soft tissues and its irregular linear spread. Early diagnosis of gas gangrene complicating a gunshot wound of the arm was possible.

X-Ray Diagnosis.—Films taken at intervals of from two to four hours may aid in the differentiation of gas in the soft tissues produced by clostridial invasion from that due to mechanical or chemical causes. They have been of practical value in the detection of early or incipient gas gangrene, permitting a positive diagnosis 24 hours or more earlier than that possible by the clinical findings alone in our experience. If the visible gas increases in amount or presents a linear spread along the muscle and fascial planes, an early diagnosis of gas gangrene can be made (Fig. 4). In far-advanced cases large quantities of gas can be visualized in the muscular tissues by x-ray examination (Fig. 5).

Fig. 5.—Far-advanced case of gas gangrene (illustrated in Fig. 3), showing extensive and obvious infiltration of muscles of the leg and thigh by gas produced by the infection.

Crepitation in tissues about a wound occasionally is not produced by bacteria. Cases in which air has been sucked into the tissues by penetrating or perforating missiles have been confused with true gas gangrene occasionally. In other instances the irrigation of wound tracts by hydrogen peroxide or benzene has caused the development of gas bubbles in tissues, which results in subcutaneous crepitation or the visualization of these bubbles on x-ray films.

Current Problems in the Prophylaxis of Gas Gangrene

Although there is considerable evidence that the prophylactic administration of gas gangrene antitoxin at the time of injury or shortly thereafter is of little or no practical value in the prevention of clinical gas gangrene, the majority of surgeons continue to give it at the time of injury. We discontinued the use of gas gangrene antitoxin prophylactically in 1943. More recently, it has been recommended by the Subcommittee on Trauma of the National Research Council and by the Department of Defense that gas gangrene antitoxin not be given at the time of injury because of the ineffectiveness of this agent in preventing the disease.

Early and adequate surgery is still the most effective means of preventing gas gangrene, and recent experimental and clinical evidence has indicated that antibiotic

therapy alone cannot be relied upon to prevent the occurrence of clostridial myositis.

Through the cooperative effort of the Department of Biochemistry and the Department of Surgery of the University of Cincinnati, an effective toxoid for C. welchii and C. novyi [4,5] has been developed and shown to be effective in preventing the occurrence of experimental gas gangrene in animals. Medical students have been injected with two or three injections of these toxoids and have shown satisfactory response with adequate antitoxin levels. Although these toxoids have been developed and proved in animals, they have not been made available to clinical surgeons as yet.

Problems in the Treatment of Established Gangrene

The principal problem in the treatment of established gas gangrene arises from delay in the recognition of this condition. The rapid spreading nature of this infection may cause an irreversible process to develop within a matter of a relatively few hours, and a delay of 24 or more hours may cause death of the patient.

Delay in operative treatment is frequently an important factor, resulting either from the surgeon's indifference to the rapid spreading nature of this infection or from his inability to obtain the operating-room facilities otherwise occupied at that time. Recently, a delay of three hours occurred during the admission of a patient with gas gangrene of the shoulder girdle. Extensive spread, overwhelming infection, and death occurred during this period.

Antisera.—There is some evidence that the use of antitoxin in conjunction with adequate surgery aids in the control of the associated toxemia. However, many surgeons doubt the efficacy of gas gangrene antitoxin. The essential objective of the use of antitoxin has been the prevention of death from toxemia by therapeutic doses, given at intervals of four to six hours, until surgery or antibiotic therapy can control the infection. The recommended intravenous injection of a therapeutic dose consists of 27,000 units of C. welchii antitoxin, 13,500 units of C. septique, and 27,000 units of C. novyi repeated at intervals of four to six hours. Thirteen of the 42 cases received gas gangrene antitoxin in varying doses. The mortality of the patients treated with antitoxin was 31% compared with 50% for those not receiving it.

Antibiotic Therapy.—Experimental and clinical evidence has indicated that penicillin is of value only when given in massive doses of 1,000,000 units every three hours, intramuscularly or intravenously.[6,7] Other experimental evidence indicates that the tetracyclines are the drugs of choice in this condition, chlortetracycline (Aureomycin) and oxytetracycline (Terramycin) being preferable. Chloramphenicol (Chloromycetin) is also of value, but other antibiotic agents are of limited usefulness.

Supportive Treatment.—The need for adequate supportive measures in the management of patients with gas gangrene is often overlooked. These measures include daily blood transfusions, maintenance of fluid and electrolyte balance, adequate immobilization of the infected injured parts, oxygen therapy, and relief of pain. Frequent blood transfusions help to correct the profound hemolytic anemia which may be present in this condition. Care must be taken, however, not to produce pulmonary edema in the face of the impaired circulation.

Summary

From an analysis of these cases and other available information, the effective methods for the treatment of established clostridial myositis, or true gas gangrene, may be summarized as follows.

1. Radical operative treatment, as soon after diagnosis as possible, consisting of multiple incisions and fasciotomy for decompression and drainage of the fascial compartments, excision of the involved muscles, or open amputation when necessary.

2. Adequate immobilization of the affected part.

3. The injection of penicillin intravenously in large doses of 1,000,000 units or more every three hours before and after operative treatment.

4. The use of one of the tetracyclines, chlortetracycline or oxytetracycline preferably, in doses of 500 mg. administered intravenously every four to six hours.

5. Administration of polyvalent gas gangrene antitoxin before and after surgery, 50,000 units being given every 4 to 6 hours for 24 to 48 hours in patients with profound toxemia and hypotension.

6. Adequate supportive therapy.

7. A delay in performing secondary operative procedures to facilitate healing, or to restore function of the wounded extremity, until the infection has been brought under control completely.

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REFERENCES

1. Altemeier, W. A., and Furste, W. L.: Gas Gangrene, Internat. Abstr. Surg. 84:507, 1947; in Surg. Gynec. & Obst., June, 1947.

2. Lindberg, R.: Bacterial Flora of Korean War Wounds, Personal communication to the senior author.

3. Altemeier, W. A.: Rapid Identification of Clostridium Welchii in Accidental Wounds, Surg. Gynec. & Obst. 78:411 (April) 1944.

4. Altemeier, W. A.; Furste, W. L.; Culbertson, W. R.; Wadsworth, C. L.; Tytell, A. A.; Logan, M. A., and Tytell, A. G.: Toxoid Immunization in Experimental Gas Gangrene, Ann. Surg. 126:509 (Oct.) 1947.

5. Altemeier, W. A.; Coith, R.; Sherman, R.; Logan, M. A., and Tytell, A.: Toxoid Immunization of Experimental Gas Gangrene, A. M. A. Arch. Surg. 65:633 (Oct.) 1952.

6. Altemeier, W. A.; Furste, W. L., and Culbertson, W. R.: Chemotherapy in Gas Gangrene, Arch. Surg. 55:668 (Dec.) 1947.

7. Altemeier, W. A.; McMurrin, J. A., and Alt, L. P.: Chloromycetin and Aureomycin in Experimental Gas Gangrene, Surgery 28:621 (Oct.) 1950.

The Work of Breathing During Surgical Operations

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Previous studies have suggested that the ventilatory volume requirement during anesthesia for surgical operations is considerably in excess of that required while the subject is in the usual preanesthetic state.[1-10] Unrecognized deficiency in carbon dioxide absorption has undoubtedly partially contributed to this requirement.[11] The lung-thorax compliance has been shown to be altered during anesthesia[12,13] and to be a pertinent factor in relating ventilatory volume to respiratory tract pressure. The work required to effect the desired ventilatory adequacy is to be considered in this paper.

The total work of breathing in patients with normal and with diseased cardiorespiratory systems, made before, during, and after general anesthesia for surgical operations, has been calculated from measurements of elastic resistance (reciprocal of lung-thorax compliance) and nonelastic resistance to breathing. The effects of various factors on the work of breathing have been considered. The changes in lung-thorax compliance that were found to occur have been previously reported in detail.[12,13]

The methods of measuring the work of breathing fall into three main groups. The first consists of measurement of the increased oxygen consumption during hyperventilation.[14] The second consists of recording the intrapleural or intraesophageal pressure and the tidal volume or rate of air flow.[15-17] Plotting volume change directly against pressure change permits measurement of the work of breathing by the lung but does not measure the work involved in moving the chest wall and adjacent viscera.[18,19] The third method uses the tank-type respirator. Determination of the pressure in the respiratory tract and concomitant volume changes of the lungs during passive respiration permits calculation of the total work required for ventilation.[20,21] The effect of restricting forces on the chest wall and diaphragm during general anesthesia for surgical operations assumes increased importance, and therefore measurement of the total work of breathing is desirable. The two methods permitting this are not readily applicable during surgical operations. For these reasons a method of calculating the work of breathing, rather than direct measurement, was used in this study.

Methods and Surgical Material

The work of breathing was calculated from the equations derived by Otis, Fenn, and Rahn.[21] The total force required for breathing may be represented by the equation $P_E = KV + Pn$.

P_E is the total force required; KV is the total elastic resistance to breathing; K is the elastance expressed as centimeters of H_2O per liter (reciprocal of lung-thorax compliance); V is the lung volume, and Pn is the total viscous and turbulent resistance to breathing or the nonelastic resistance to breathing.

The lung-thorax compliance was measured by a method that has been described in detail.[12,13] The method used in the unanesthetized patients was basically that described by Rahn, Otis, Chadwick, and Fenn.[22,23] The unanesthetized patient was allowed to inspire; the airway was occluded;

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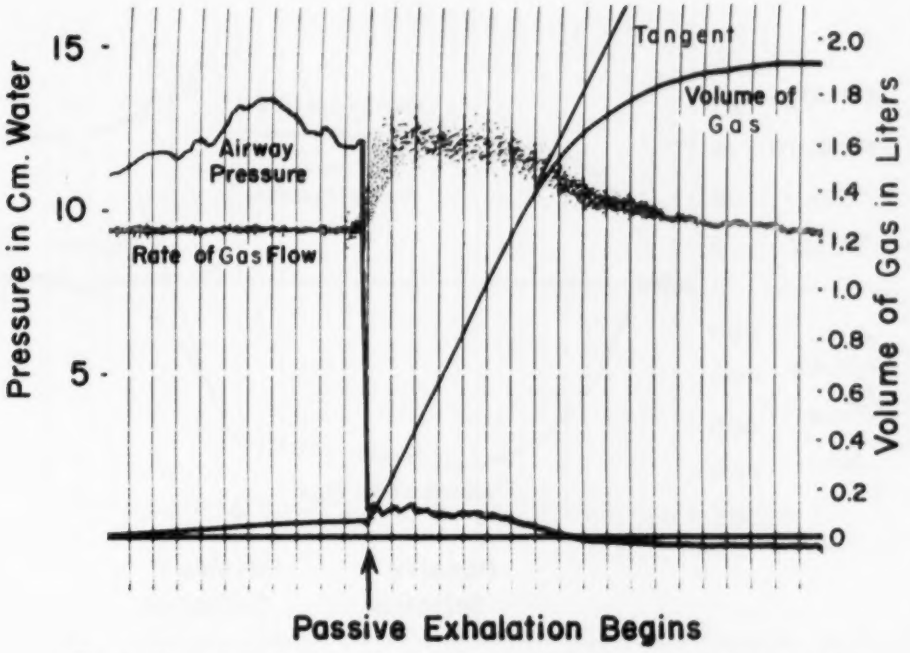

Fig. 1.—Unanesthetized subject. Vertical lines indicate 0.2-second intervals. The 0.2-second interval beginning with passive exhalation was retouched by the artist for greater clarity.

and the airway pressure was measured with a pressure transducer (Statham P23A) during a state of voluntary complete relaxation. The airway occlusion was released, and the volume of passively exhaled gas was measured by electronic integration of rate of gas flow against time as it passed through a pneumotachograph. A permanent photographic record was made of all measurements as they appeared on the oscilloscope. A sample record is shown in Figure 1. This measurement was repeated 20 to 25 times with the use of different volumes of gas, and a volume/pressure curve was plotted, as shown in Figure 2. The average value of V/P was termed lung-thorax compliance and was expressed as milliliters of gas per centimeter of H_2O pressure change. Multiple readings were required to obtain statistically significant results because of the scattering of the plotted points. "Training" of the patients was not used to increase the degree of relaxation, nor were any "inaccurate" readings discarded once the study was started.

The airway pressure was measured during anesthesia as the lungs were inflated

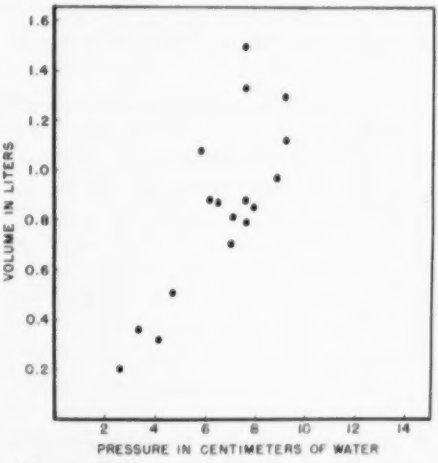

Fig. 2.—Volume/pressure relationship in unanesthetized subject.

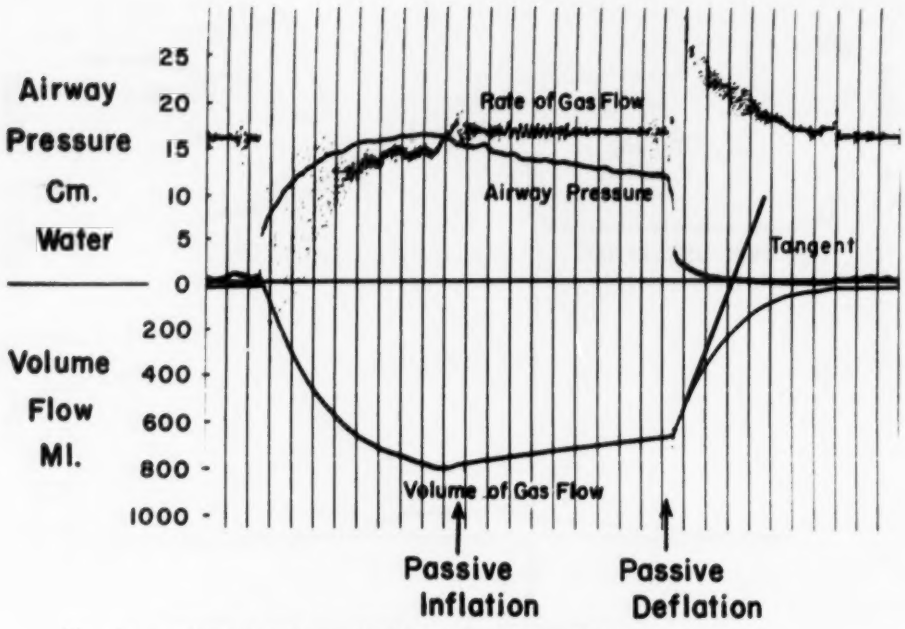

Fig. 3.—Anesthetized subject. Vertical lines indicate 0.2-second intervals.

with oxygen in a period of apnea produced by hyperventilation or by neuromuscular blocking agents. The airway was occluded, and intratracheal pressure was measured. The airway occlusion was released, and the amount of passively exhaled gas was measured. A sample record is shown in Figure 3. This was repeated three to six times in succession, the lungs being inflated with different volumes of oxygen but all factors influencing lung-thorax compliance being kept as nearly constant as possible during this time. Immediately after this, the factor under investigation was changed, and three to six more measurements were taken in succession. The volume/pressure values during inflation and deflation (6 to 12 readings) were averaged to give the mean

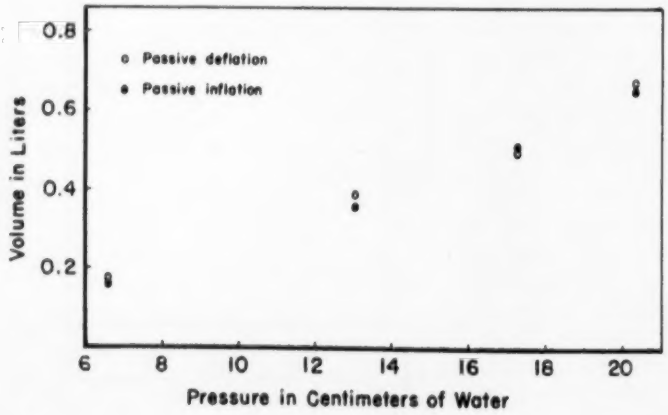

Fig. 4.—Volume/pressure relationship in anesthetized subject.

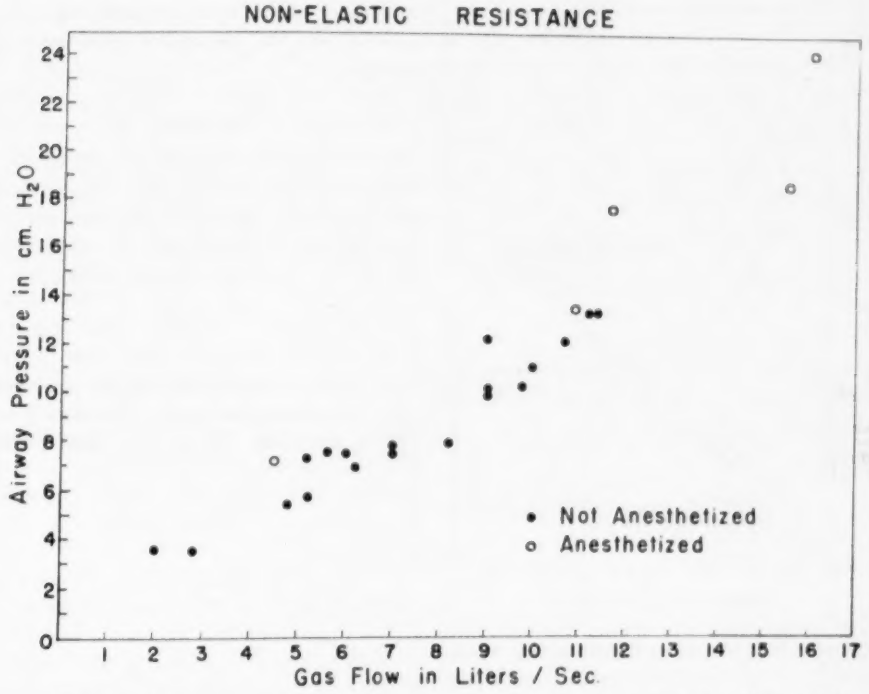

Fig. 5.—Airway pressure/gas volume flow relationship in an anesthetized subject and in an unanesthetized subject.

lung-thorax compliance for each factor measured. The plotted points were virtually linear during anesthesia, as shown in Figure 4.

The nonelastic resistance to breathing was measured by the method described by Comroe, Nisell, and Nims [24]—resistance = pressure/flow. The resistance can be calculated at any point during expiration from the slope of the line tangent to the volume time record. The point used to measure the nonelastic resistance was the start of expiration, as shown by the tangent drawn in Figure 1 and in Figure 3. The same point, the beginning of expiration, was used each time to permit comparison of the values obtained. The pressure/flow curve was plotted as shown in Figure 5. The average P/F value was termed the nonelastic resistance and was expressed as centimeters of H_2O per liter per second.

Otis, Fenn, and Rahn [21] estimated the elastic resistance and the total resistance to breathing from measurements obtained on relaxed, normal, human subjects ventilated by a tank-type respirator. They derived the following equation:

$$\text{Work per unit time} = \tfrac{1}{2}Kf\left(\frac{\dot{V}_A}{f}+V_D\right)^2+$$

$$\tfrac{1}{4}K'\pi^2(\dot{V}_A+fV_D)^2+2/3K''\pi^2(\dot{V}_A+fV_D)^2$$

This permitted estimation of the elastic and nonelastic components of the total work of breathing, their relationship to the frequency of breathing, and the volume of alveolar ventilation. An example is shown in Figure 6 with an alveolar ventilation of 6 liters per minute and a dead space of 200 ml. The values for the work of breathing in the normal subject established by Otis, Fenn, and Rahn [21] are assumed to apply to the group of normal controls in the present study. Calculation of the total work of breathing and the elastic and nonelastic components of the other subjects, with comparison with the normal controls,

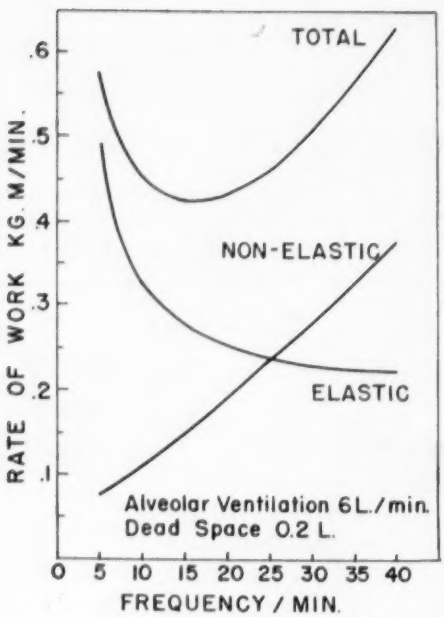

Fig. 6.—Relationship of elastic, nonelastic, and total work of breathing to respiratory rate. Modified from Otis, Fenn, and Rahn.

was made on the basis of the equation, $P_E = KV + Pn$. The value for work that is obtained by this method is calculated rather than directly measured. The relative changes in the work required should be reflected, since the elastic component of the work of breathing varies inversely as the lung-thorax compliance and the nonelastic component of the work of breathing varies directly as the nonelastic resistance to breathing.

Results

1. *Resistance to Breathing of Controls.*—The elastic and the nonelastic resistance to breathing was measured in nine normal, unanesthetized subjects on 32 separate occasions to establish normal values. The measurements were made in the supine position without sedation. The subjects were healthy, average-sized, and active. They formed the control group to which later comparisons are made. The results are shown in Table 1. The average elastic resistance to breathing was 4.8 cm. of H_2O per liter. The average nonelastic resistance to breathing was 8.2 cm. of H_2O per liter per second.

2. *Effect of Cardiac Disease and Pulmonary Disease on Resistance to Breathing.*—The elastic and the nonelastic resistance to breathing was measured in nine unanesthetized patients with cardiac disease and in nine unanesthetized patients with pulmonary disease. All measurements were made in the supine position without sedation and before surgical operation. The results are shown in Table 1. The average elastic resistance to breathing in the group with cardiac disease was 8.0 cm. of H_2O per liter, 170% of the control group. The aver-

Table 1.—*Effect of Cardiac Disease and Pulmonary Disease on Resistance to Breathing* *

Nine Normal Controls		Cardiac Disease			Pulmonary Disease		
Elastic Resistance, Cm. H_2O/L.	Nonelastic Resistance, Cm. H_2O/L/Sec.	Disease	Elastic Resistance, Cm. H_2O/L.	Nonelastic Resistance, Cm. H_2O/L/Sec.	Disease	Elastic Resistance, Cm. H_2O/L.	Nonelastic Resistance, Cm. H_2O/L/Sec.
2.9	4.8	Mitral stenosis	4.5	7.3	Bronchiectasis	12.5	15.1
2.5	5.9	Mitral stenosis	7.1	13.2	Bronchiectasis	3.4	7.1
7.7	9.1	Mitral stenosis	14.3	13.8	Bronchiectasis; empyema	4.8	10.9
6.7	8.6	Mitral stenosis	10.0	11.1	Lung carcinoma	7.7	8.7
3.9	10.2	Mitral stenosis	4.8	8.5	Lung carcinoma	11.1	13.5
5.9	8.5	Patent ductus	12.5	13.9	Lung carcinoma	9.1	11.3
4.8	9.7	Patent ductus	4.5	10.3	Metastases to lung	4.2	12.7
3.2	7.0	Pulmonic stenosis	5.9	10.4	Emphysemae, cor pulmonale	11.1	29.1
5.9	9.9	Pulmonic stenosis	8.3	10.8	Emphysema; cor pulmonale	16.7	24.3
Average 4.8	Average 8.2	9 Cases	Average 8.0 167% of controls	Average 11.0 134% of controls	9 Cases	Average 9.0 187% of controls	Average 14.7 180% of controls

* Unanesthetized.

age elastic resistance to breathing in the group with pulmonary disease was 9.0 cm. of H_2O per liter, 190% of the control group. The average nonelastic resistance to breathing in the group with cardiac disease was 11.0 cm. of H_2O per liter per second, 130% of the control group. The average nonelastic resistance to breathing in the group with pulmonary disease was 14.7 cm. of H_2O per liter per second, 180% of the control group.

3. *Work of Breathing of Controls.*—The average work total of breathing in the group of nine normal controls was assumed to be the same as the average work of breathing obtained by Otis, Fenn, and Rahn in their study of relaxed, normal, human subjects ventilated by a tank-type respirator.[21] As is shown in Figure 6, the average elastic work of breathing was 0.25 kg-m. per minute, 58% of the total work of breathing when the alveolar ventilation was 6 liters per minute, the dead space 200 ml., and the frequency 20 per minute. The nonelastic work of breathing was 0.18 kg-m. per minute, 42% of the total work. The total work of breathing was 0.43 kg-m. per minute under these conditions.

4. *Effect of Cardiac Disease and Pulmonary Disease on Work of Breathing.*—The work of breathing was calculated in the group of nine unanesthetized patients with cardiac disease and in the group of nine unanesthetized patients with pulmonary disease on the basis of the measurements of the resistance to breathing shown in Table 1. The results with an alveolar ventilation of 6 liters per minute, a dead space of 200 ml., and a frequency of 20 per minute are shown in Table 2. Average elastic work of breathing in the group with cardiac disease was 0.42 kg-m. per minute, 170% of the control group and 64% of the total work of breathing. The average nonelastic work of breathing in the group with cardiac disease was 0.24 kg-m. per minute, 130% of the control group and 36% of the total work of breathing. The average total work of breathing in the group with cardiac disease was 0.66 kg-m. per minute, 150% of the control group.

The average elastic work of breathing in the group with pulmonary disease was 0.47 kg-m. per minute, 190% of the control group and 60% of the total work of breathing. The average nonelastic work of breathing in the group with pulmonary disease was 0.32 kg-m. per minute, 180% of the control group and 40% of the total work of breathing. The average total work of breathing in the group with pulmonary disease was 0.79 kg-m. per minute, 180% of the control group.

5. *Resistance to Breathing in the Maximum Work of Breathing During Surgery.* The resistance to breathing was measured in 25 patients on 147 different occasions in widely varying circumstances during general anesthesia for surgical operations. The type of surgery varied. The elastic and the nonelastic resistance to breathing found during the maximum work of breathing encountered for each patient is shown in Table 3. The average elastic resistance in these circumstances was 45 cm. of H_2O per liter. The elastic resistance averaged 930% of the normal control group and in one case was 4170% of the normal control group. The average nonelastic resistance was 17.6 cm. of H_2O per liter per second in the same circumstances. The nonelastic resistance averaged 220% of the

TABLE 2.—*Effect of Cardiac Disease and Pulmonary Disease on Work of Breathing* *

Subjects	Cases, No.	Elastic Work of Breathing		Nonelastic Work of Breathing		Total Work of Breathing, Kg-M/Min.
		Kg-M/Min.	Per Cent of Total Work	Kg-M/Min.	Per Cent of Total Work	
Controls	9	0.25	58	0.18	42	0.43
Cardiac disease	9	0.42	64	0.24	36	0.66
Pulmonary disease	9	0.47	60	0.32	40	0.79

* Alveolar ventilation, 6 liters per minute; dead space, 200 ml.; frequency, 20 per minute; unanesthetized.

TABLE 3.—*Resistance to Breathing in Maximum Work of Breathing During Surgery*

Case, No.	Operation	Elastic Resistance		Nonelastic Resistance	
		Cm.H_2O/L.	Per Cent of Normal Controls	Cm.H_2O/L/Sec.	Per Cent of Normal Controls
1	Pneumonectomy	30	630	25.9	320
2	Pneumonectomy	50	1,040	22.7	280
3	Lobectomy	48	1,000	15.7	190
4	Lobectomy	26	540	19.4	240
5	Excision of bullae	30	630	17.7	220
6	Mitral valvotomy	26	540	15.3	190
7	Mitral valvotomy	24	500	8.7	110
8	Mitral valvotomy	83	1,730	22.2	270
9	Mitral valvotomy	40	830	16.5	200
10	Pulmonic valvotomy	21	440	14.1	170
11	Pulmonic valvotomy	26	540	12.4	150
12	Division patent ductus	40	830	17.7	220
13	Thoracotomy	30	630	15.1	180
14	Nephrectomy	111	2,310	34.5	420
15	Duodenojejunostomy	30	630	15.1	180
16	Exploratory laparotomy	53	1,100	23.4	290
17	Subtotal gastrectomy	35	730	15.6	190
18	Cholecystectomy; common duct exploration	45	940	14.3	170
19	Exploratory laparotomy	43	900	14.1	170
20	Cystocele and rectocele repair	21	440	8.3	100
21	Cystocele and rectocele repair	33	690	21.8	270
22	Vaginal hysterectomy	21	440	11.1	140
23	Vaginal hysterectomy; cystocele and rectocele repair	22	460	12.1	150
24	Iliac artery graft	200	4,170	31.7	390
25	AP resection of rectum	30	630	15.0	180
		Average 45	Average 930	Average 17.6	Average 220

normal control group, with the highest being 420% of the control group.

6. *Maximum Work of Breathing Required During Surgery.*—The work of breathing was calculated in 25 patients on 147 different occasions in widely varying circumstances during general anesthesia for surgical operations. The maximum work of breathing encountered in each patient, based on an alveolar ventilation of 6 liters per minuute, a dead space of 200 ml., and a frequency of 20 per minute, is shown in Table 4. The elastic and the nonelastic resistance found in each case is shown in Table 3. The average maximum total work of breathing for these 25 patients was 2.72 kg-m. per minute and averaged 620% of the control group. The average elastic work of breathing was 2.33 kg-m. per minute and averaged 84% of the total work. The average nonelastic work of breathing was 0.39 kg-m. per minute and averaged only 16% of the total work.

An average of the three calculations for maximum total work of breathing encountered in each individual is also shown in Table 4. The average total work of breathing was 2.17 kg-m. per minute, 510% of the control group.

7. *Effect of General Anesthesia on Resistance to Breathing.*—The elastic and the nonelastic resistance to breathing was measured in 19 unanesthetized, unsedated, supine patients on the day preceding surgery and again in the supine, anesthetized patient immediately preceding the initiation of the operation. Several different types of general anesthetic agents were used. Apnea was obtained either by hyperventilation or by a combination of hyperventilation and neuromuscular blocking agents. The results are shown in Table 5. There was a large, consistent increase in the elastic resistance in the anesthetized state, which averaged 280% above that of the preanesthetized state. There was a relatively slight increase of 17% in the nonelastic resistance in the anesthetized state.

8. *Effect of General Anesthesia on Work of Breathing.*—The work of breathing was calculated in 19 unanesthetized, unsedated, supine patients on the day preceding surgery and again in the supine, anesthetized patient preceding the initiation of the operation. Several different types of general anesthetic agents were used. The calculations were based on the measurements of resistance to breathing shown in Table 5

TABLE 4.—*Maximum Work of Breathing Required During Surgery* *

Case, No.	Elastic Work		Nonelastic Work		Total Work of Breathing			
					Maximum Measurement		Average of Three Maximum Measurements	
	Kg-M/Min.	Per Cent of Total Work	Kg-M/Min.	Per Cent of Total Work	Kg-M/Min.	Per Cent of Controls	Kg-M/Min.	Per Cent of Controls
1	1.57	73	0.58	27	2.15	500	1.86	430
2	2.60	84	0.50	16	3.10	720	2.64	610
3	2.50	88	0.34	12	2.84	430	2.25	520
4	1.35	76	0.43	24	1.78	410	1.54	360
5	1.57	80	0.40	20	1.97	460	1.75	410
6	1.35	80	0.34	20	1.69	390	1.57	370
7	1.25	86	0.20	14	1.45	340	1.41	330
8	4.33	90	0.49	10	4.82	1,120	2.97	690
9	2.07	85	0.36	15	2.43	570	2.26	530
10	1.10	78	0.31	22	1.41	330	1.15	270
11	1.35	83	0.27	17	1.62	380	1.39	320
12	2.08	84	0.40	16	2.48	570	2.31	550
13	1.57	83	0.32	17	1.89	440	1.52	350
14	5.78	89	0.76	11	6.54	1,520	4.53	1,060
15	1.57	83	0.32	17	1.89	440	1.71	400
16	2.75	84	0.52	16	3.27	760	2.61	610
17	1.82	84	0.34	16	2.16	500	2.02	470
18	2.35	88	0.31	12	2.66	620	2.16	500
19	2.25	88	0.31	12	2.56	600	2.18	510
20	1.10	86	0.18	14	1.28	300	1.19	280
21	1.72	78	0.49	22	2.21	510	2.15	500
22	1.10	82	0.25	18	1.35	310	1.30	300
23	1.15	81	0.27	19	1.42	330	1.38	320
24	10.40	94	0.70	6	11.10	2,580	6.52	1,520
25	1.57	83	0.32	17	1.89	440	1.79	420
	Average 2.33	Average 84	Average 0.39	Average 16	Average 2.72	Average 620	Average 2.17	Average 510

* Alveolar ventilation, 6 liters per minute; dead space, 200 ml.; frequency, 20 per minute.

on the basis of an alveolar ventilation of 6 liters per minute, a dead space of 200 ml., and a frequency of 20 per minute. The results are shown in Table 6. In the anesthetized state there was a rather large increase in the total work of breathing, with an average increase of 170%. The major portion of this increase in the total work of breathing in the anesthetized patient occurred in the elastic work of breathing. The elastic work in the unanesthetized state averaged 59% of the total work but increased to 80% of the total work in the anesthetized state. The nonelastic work accordingly fell from 41% of the total work in the unanesthetized state to 20% of the total work in the anesthetized state.

9. *Effect of Other Factors on Breathing Resistance and Work.*—Factors during operation influencing the work of breathing

TABLE 5.—*Effect of General Anesthesia on Resistance to Breathing*

Case, No.	Anesthetic Agent *	Type of Apnea †	Elastic Resistance			Nonelastic Resistance		
			Unanesthetized, ‡ Cm. H_2O/L.	Anesthetized, § Cm. H_2O/L.	Change, per Cent	Unanesthetized, ‡ Cm. H_2O/L/Sec.	Anesthetized, § Cm. H_2O/L/Sec.	Change, per Cent
1	E	H	4.2	13.9	+230	10.0	11.0	+10
2	T, E	H, S	11.1	20.0	+80	13.5	24.1	+78
3	T, E	H, S	4.8	16.1	+240	10.9	8.3	−24
4	T, E	H, S	7.1	23.8	+240	13.2	12.4	−6
5	T, C, E	H, D	5.9	21.3	+260	10.4	14.1	+36
6	T, E	H, D	8.3	20.4	+150	10.8	11.3	+5
7	C	H	4.8	20.4	+330	8.5	8.3	−2
8	C, E	H	11.1	16.4	+50	29.1	30.0	+3
9	C	H, S	4.5	34.5	+670	10.3	13.7	+33
10	C	H	4.2	17.6	+320	12.7	9.1	−28
11	C	H	3.5	21.7	+520	7.1	11.2	+58
12	C	H	10.0	34.5	+250	11.1	12.6	+14
13	T, C	H, S	13.0	111.0	+750	13.1	34.5	+163
14	N, E	H	25.0	30.3	+20	28.3	15.6	−45
15	.....	H, S	10.0	23.8	+140	13.9	12.9	−7
16	T, N	G	6.7	20.0	+200	13.6	15.0	+10
17	T, C, E	H, D	5.3	23.8	+350	10.9	9.9	−9
18	C, E	H	9.1	25.0	+180	16.6	16.0	−4
19	C, E	H, D	4.2	16.4	+290	8.0	10.8	+35
		Average			+280			+17

* E=ether; T=thiopental; C=cyclopropane; N=N_2O-O_2.
† H=hyperventilation; S=succinylcholine; D=decamethonium bromide (Syncurine); G=gallamine (Flaxedil) triethiodide.
‡ All measurements taken in supine position the day preceding operation.
§ All measurements taken in supine position before start of operation.

TABLE 6.—*Effect of General Anesthesia on Work of Breathing* *

Case, No.	Elastic Work				Nonelastic Work				Total Work		
	Unanesthetized		Anesthetized		Unanesthetized		Anesthetized		Unanesthetized, Kg-M/Min.	Anesthetized, Kg-M/Min.	Change, per Cent
	Kg-M/Min.	Per Cent of Total Work	Kg-M/Min.	Per Cent of Total Work	Kg-M/Min.	Per Cent of Total Work	Kg-M/Min.	Per Cent of Total Work			
1	0.22	50	0.73	76	0.22	50	0.23	24	0.44	0.96	+120
2	0.58	67	1.65	67	0.29	33	0.52	33	0.87	1.57	+80
3	0.25	52	0.85	83	0.23	48	0.18	17	0.48	1.03	+110
4	0.38	57	1.25	82	0.29	43	0.27	18	0.67	1.52	+130
5	0.50	57	1.10	78	0.23	43	0.31	22	0.53	1.41	+170
6	0.43	65	1.07	81	0.23	35	0.25	19	0.66	1.32	+100
7	0.25	58	1.07	86	0.18	42	0.18	14	0.43	1.25	+190
8	0.58	47	0.85	56	0.65	53	0.67	44	1.23	1.52	+20
9	0.24	51	1.80	85	0.23	49	0.31	15	0.47	2.11	+350
10	0.22	43	0.93	82	0.29	57	0.20	18	0.51	1.13	+120
11	0.18	53	1.12	82	0.16	47	0.25	18	0.34	1.37	+300
12	0.53	68	1.80	87	0.25	32	0.27	13	0.78	2.07	+170
13	0.68	70	5.78	89	0.29	30	0.76	11	0.97	6.54	+580
14	1.30	67	1.57	71	0.63	33	0.34	29	1.93	2.20	+10
15	0.53	63	1.25	80	0.31	37	0.29	20	0.84	1.56	+90
16	0.35	53	1.05	77	0.31	47	0.32	23	0.66	1.36	+110
17	0.28	68	1.25	84	0.23	32	0.22	16	0.41	1.48	+260
18	0.48	68	1.30	85	0.23	32	0.36	15	0.71	1.53	+120
19	0.22	55	0.85	83	0.18	45	0.23	17	0.40	1.03	+160
Average		59		80		41		20			+170

* Alveolar ventilation, 6 liters per minute; dead space, 200 ml.; frequency, 20 per minute.

were studied. As has been indicated, general anesthesia was shown to be one important factor. The effect of other factors is shown in Table 7. The calculations of the work of breathing were based on an alveolar ventilation of 6 liters per minute, a dead space of 200 ml., and a frequency of 20 per minute. During abdominal surgery in four patients there was an average increase in the total work of breathing of 16%, with a range of +6% to +25% when an arm of the assistant rested on the patient's thorax. In four patients retraction against the liver with a Deaver retractor resulted in an average increase in the total work of breathing of 24%, with a range of +2% to +61%. In five patients retraction against the liver and an arm resting on the thorax resulted in an average increase in the total work of breathing of 51%, with a range of +8% to +156%.

During thoracic surgery in seven patients there was an average increase in the total work of breathing of 17%, with a range of −10% to +82% when the shift was made from the supine to the lateral position. The increase in the amount of work correlated with the extent of the disease in the uppermost lung in the lateral position. In five patients there was an average decrease in the total work of breathing of 13%, with a range of −44% to +26% when the chest was opened and the rib spreader was put in place. In seven patients when the lung was retracted to gain exposure, there was an average increase in the total work of breathing of 32%, with a range of +1% to +132% when compared with the anesthe-

TABLE 7.—*Effect of Other Factors on Breathing Resistance and Work* *

Cases, No.	Factor	Change in Elastic Work and Resistance		Change in Nonelastic Work and Resistance		Change in Total Work	
		Average, per Cent	Range, per Cent	Average, per Cent	Range, per Cent	Average, per Cent	Range, per Cent
	Abdominal Surgery						
4	Arm on chest	+18	+ 8 to +33	−4	−17 to +5	+16	+ 6 to +25
4	Retraction against liver	+26	− 2 to +58	+24	−10 to +80	+24	+ 2 to +61
5	Retraction against liver and arm on chest	+53	+ 8 to +160	+33	− 9 to +104	+51	+ 8 to +156
	Thoracic Surgery						
7	Lateral position	+19	−13 to +88	+12	−25 to +58	+17	−10 to +82
5	Open chest	−18	−49 to +24	+6	−11 to +29	−13	−44 to +26
7	Open chest and retractor	+31	− 4 to +150	+26	− 4 to +47	+32	+ 1 to +132

* Alveolar ventilation, 6 liters per minute; dead space, 200 ml.; frequency, 20 per minute.

tized state in the lateral position prior to opening the chest. The average change and range of change in the elastic and the nonelastic work and resistance to breathing caused by these factors, studied during abdominal and thoracic surgery, are shown in Table 7.

Comment

The mechanical work done by the respiratory muscles in producing the movements of the breathing was first studied in detail by Rohrer[25-27] and later by Neergaard and Wirz,[16] Vuilleumier,[28] Bayliss and Robertson,[18] and Dean and Visscher.[19] Their studies have shown that the respiratory muscles in carrying out the breathing movements have to overcome resisting forces, which may be divided into the elastic and the nonelastic resisting forces to breathing. The lungs and thorax are elastic in their behavior and provide an elastic resistance which must be overcome to increase the volume of pulmonary gas during inspiration. The nonelastic resistance is primarily the viscous and turbulent resistance encountered by gas moving through the respiratory tract, the resistance associated with deformation of tissues, and the sliding of the adjacent organ surfaces over one another when displaced. Other relatively unimportant nonelastic resisting forces are the inertia of the system and the kinetic energy imparted to the gas.

The mechanical work done in breathing at rest normally is 0.4 to 0.5 kg-m. per minute. Assuming an efficiency of 5%, this represents a total energy requirement of about 33.7 large calories per day, or only 1% or 2% of the total resting metabolism.[21] Normally the maximum muscular power available for ventilatory effort is approximately 500 times that required for resting ventilation. This results, however, in an increased ventilatory volume of only 15 to 20 times the resting ventilation.[21] The maximal muscular effort can be continued only for short intervals.

In this study cardiac disease and pulmonary disease were found to increase the work of breathing in unanesthetized subjects. Others have reported similar findings.[29-31] Christie has correlated the subjective symptoms of dyspnea present in patients having cardiac or respiratory disease with the increase in the work of breathing.[32] In patients with mitral stenosis it is related primarily to an increase in elastic resistance to breathing.[29] This is probably due to pulmonary congestion, for experimental production of pulmonary congestion has been found to decrease significantly the distensibility of the lungs.[33,34] The increase in the work of breathing in patients with emphysema is related primarily to the increase in nonelastic resistance to breathing, although cor pulmonale is associated with an increase in both elastic and nonelastic resistance.[30,31] These findings were borne out in this study.

A significant increase in the total work of breathing during general anesthesia for surgical operations was found to occur in this study. The principal cause for this was found to be the general anesthesia itself, owing primarily to an increase in elastic resistance. Holaday and Israel reported similar findings.[35] Others have shown an increase in elastic resistance to breathing to occur during general anesthesia.[36,37] Any factor restricting the movement of the thorax, diaphragm, or lung was found to increase the total work of breathing in this study.

Other factors not measured may further increase the work of breathing during surgery. The added resistance of the anesthetic machine is to be considered, but ordinarily it is relatively insignificant.[37] The calculations of the work of breathing in this study were all based on an alveolar ventilation of 6 liters per minute. The increase in work of ventilation during surgery would be considerably higher than has been indicated, for the need for increased total volume of ventilation during surgery has been demonstrated. The effect of increased alveolar ventilation on the work of breathing is shown in Figure 7. A third

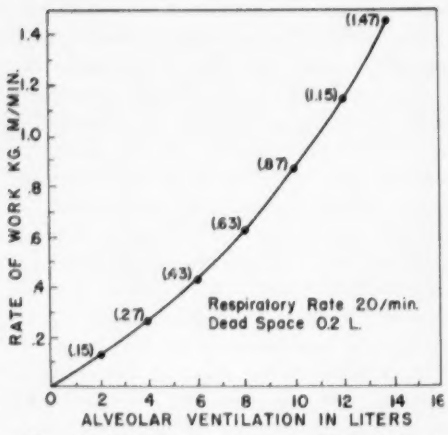

Fig. 7.—Relationship of work of breathing to alveolar volume ventilation. Calculated from equations of Otis, Fenn, and Rahn.

factor is the functional increase in elastic resistance occurring with increase in respiratory rate in emphysematous subjects.[31,38] A fourth factor is the increase in elastic resistance to breathing that may occur when tubocurarine (*d*-Tubocurarine) chloride is used as an anesthetic adjuvant.[39]

There are metabolic consequences of increased work of breathing that are to be considered. One is an increase in the oxygen cost of breathing.[40] The other is an increase in carbon dioxide production. It is theoretically possible for this increase in carbon dioxide production to be greater than can be accommodated by the increase in alveolar ventilation.[41] The variable increase in work of breathing required for adequate ventilation during general anesthesia for surgical operations appears to be a factor in the occurrence of ventilatory inadequacy and the associated respiratory acidosis.

Summary

Calculations of the work of breathing based upon measurements of the elastic and the nonelastic resistance to breathing have been made in patients with normal and with diseased cardiorespiratory systems before, during, and after general anesthesia for surgical operations.

There was an increase in the work of breathing in nine patients with cardiac disease and in nine patients with pulmonary disease when compared with a group of nine subjects with normal cardiovascular systems.

The work of breathing may increase many fold during general anesthesia for surgical operations, primarily because of an increase in the elastic work of breathing.

General anesthesia itself was a major factor producing the increased work of breathing found during general anesthesia for surgical operations.

Factors which interfered with the movement of the chest wall, lung, or diaphragm, such as an assistant's arm resting on the thorax, retraction against the liver, an arm resting on the thorax during retraction against the liver, the lateral position, or retraction against the lung, all resulted in an increase in the work of breathing.

The significance of the increased work of breathing during general anesthesia for surgical operations and its relationship to the occurrence of respiratory acidosis are discussed.

Mrs. Rose Marie Dunden gave technical assistance in the determinations reported.

Department of Surgery, University of Kansas Medical Center (3) (Dr. Allbritten)

DISCUSSION

DR. FRANK F. ALLBRITTEN JR., Kansas City, Kan.: This seems like a rather narrow approach to a problem that we have been primarily concerned about over a period of time. Stated in rather broad terms, it is to provide safe conduct through a critical period, the operative period, for the patient by more careful study of the requirements of that period.

You will note that in the material presented by Dr. Brownlee certain periods of time may not put particular work demand upon the patient. The work requirement may not be particularly great continuously, but when maximal ventilation is a requirement, large work demand may be placed upon a patient for a period of time. We have not had any measure or objective evidence of such demand until we were able to complete these studies.

There has been more of a tendency to delegate the welfare of the patient during this critical

period to the anesthesiologist. Perhaps this is a product of the additional specialization that Dr. Johnston spoke about this morning. Unfortunately, or fortunately, as the case may be, the responsibility of the patient still lies with the surgeon.

I think it behooves all of us to realize that one important factor throughout a very critical period of time is the volume of ventilation given to the patient. I am repeatedly impressed with the period of apnea permitted by many anesthesiologists during the period of intubation, while they are occupied with an intravenous infusion or other procedures in the operating room. My good friend Julian Johnson has frequently told the anesthesiologist he must hold his breath for any period of time during which he is not ventilating the patient. This significantly reduces periods of apnea for the patient.

To us this has been a most revealing study on the demand imposed upon the patient for any given period of time during an operative procedure. We believe it may be an additional factor in explaining the inadequate ventilation which frequently occurs during a given operative procedure.

REFERENCES

1. Taylor, F. H., and Roos, A.: Disturbances in Acid-Base Balance During Ether Anesthesia, J. Thoracic Surg. 20:289-295 (Aug.) 1950.

2. Beecher, H. K., and Murphy, A. J.: Acidosis During Thoracic Surgery, J. Thoracic Surg. 19: 50-70 (Jan.) 1950.

3. Buckley, J. J.; Van Bergen, F. H.; Dobkin, A. B.; Brown, E. B., Jr.; Miller, F. A., and Varco, R. L.: Postanesthetic Hypotension Following Cyclopropane: Its Relationship to Hypercapnia, Anesthesiology 14:226-237 (May) 1953.

4. Dripps, R. D.: Immediate Decrease in Blood Pressure Seen at Conclusion of Cyclopropane Anesthesia: "Cyclopropane Shock," Anesthesiology 8:15-35 (Jan.) 1947.

5. Etsten, B. E., and Messer, A. C.: Respiratory Acidosis During Intrathoracic Surgery: The (Overholt) Prone Position, J. Thoracic Surg. 25:286-299 (March) 1953.

6. Gabbard, J. B.; Roos, A.; Eastwood, D. E., and Burford, F. H.: Effect of Ether Anesthesia upon Alveolar Ventilation and Acid-Base Balance in Man, Ann. Surg. 136:680-690 (Oct.) 1952.

7. Gibbon, J. H., Jr.; Allbritten, F. F., Jr.; Stayman, J. W., Jr., and Judd, J. M.: Clinical Study of Respiratory Exchange During Prolonged Operations with an Open Thorax, Ann. Surg. 132:611-625 (Oct.) 1950.

8. Ellison, R. G.; Ellison, L. T., and Hamilton, W. F.: Analysis of Respiratory Acidosis During Anesthesia, Ann. Surg. 141:375-382 (March) 1955.

9. Allbritten, F. F., Jr.; Haupt, G. J., and Amadeo, J. H.: Change in Pulmonary Alveolar Ventilation Achieved by Aiding the Deflation Phase of Respiration During Anesthesia for Surgical Operations, Ann. Surg. 140:569-582 (Oct.) 1954.

10. Stead, W. W.; Martin, F. E., and Jensen, N. K.: Physiologic Studies Following Thoracic Surgery: IV. Mechanism of the Development of Acidosis During Anesthesia, J. Thoracic Surg. 25:435-447 (May) 1953.

11. Nealon, T. F., Jr.; Haupt, G. J.; Chase, H. F.; Price, J. E., and Gibbon, J. H., Jr.: Inefficient Carbon Dioxide Absorption Requiring Increased Pulmonary Ventilation During Operations, J. Thoracic Surg. 32:464-474 (Oct.) 1956.

12. Brownlee, W. E., and Allbritten, F. F., Jr.: Significance of the Lung-Thorax Compliance in Surgical Operations, A. M. A. Arch. Surg. 72: 893-900 (June) 1956.

13. Brownlee, W. E., and Allbritten, F. F., Jr.: Significance of the Lung-Thorax Compliance in Ventilation During Thoracic Surgery, J. Thoracic Surg. 32:454-463 (Oct.) 1956.

14. Liljestrand, G.: Untersuchungen über die Atmungsarbeit, Skandinav. Arch. Physiol. 35:199-293, 1918.

15. Christie, R. V., and McIntosh, C. A.: Measurement of the Intrapleural Pressure in Man and Its Significance, J. Clin. Invest. 13:279-294 (March) 1934.

16. von Neergaard, K., and Wirz, K.: Über eine Methode zur Messung der Lungenelastizität am lebenden Menschen, insbesondere beim Emphysem, Ztschr. klin. Med. 105:35-50, 1927.

17. Paine, J. R.: Clinical Measurement of Pulmonary Elasticity, J. Thoracic Surg. 9:550-567 (June) 1940.

18. Bayliss, L. E., and Robertson, G. W.: Visco-Elastic Properties of the Lungs, Quart. J. Exper. Physiol. 29:27-47 (March) 1939.

19. Dean, R. B., and Visscher, M. B.: Kinetics of Lung Ventilation, Am. J. Physiol. 134:450-468 (Oct.) 1941.

20. Ferris, B. G., Jr.; Mead, J.; Whittenberger, J. L., and Saxton, G. A., Jr.: Pulmonary Function in Convalescent Poliomyelitic Patients: Compliance of the Lungs and Thorax, New England J. Med. 247:390-393 (Sept. 11) 1952.

21. Otis, A. B.; Fenn, W. O., and Rahn, H.: Mechanics of Breathing in Man, J. Appl. Physiol. 2:592-607 (May) 1950.

22. Rahn, H.; Otis, A. B.; Chadwick, L. E., and Fenn, W. O.: Pressure-Volume Diagram of the Thorax and Lung, Am. J. Physiol. 146:161-178 (May) 1946.

23. Otis, A. B.; Rahn, H., and Fenn, W. O.: Venous Pressure Changes Associated with Positive Intra-Pulmonary Pressures: Their Relationship to the Distensibility of the Lung, Am. J. Physiol. 146:307-317 (May) 1946.

24. Comroe, J. H., Jr.; Nisell, O. I., and Nims, R. G.: Simple Method for Concurrent Measurement of Compliance and Resistance to Breathing in Anesthetized Animals and Man, J. Appl. Physiol. 7:225-228 (Sept.) 1954.

25. Rohrer, F.: Der Strömungswiderstand in den menschlichen Atemwegen und der Einfluss der unregelmässigen Verzweigung des Bronchialsystems auf den Atmungsverlauf verschiedenen Lungenbezirken, Arch. ges. Physiol. 162:225-229, 1915.

26. Rohrer, F.: Der Zusammenhang der Atemkräfte und ihre abhängigkeit vom Dehnungzustand der Atmungsorgane, Arch. ges. Physiol. 165:419, 1916.

27. Rohrer, F.; Nakasone, K., and Wirz, K.: Physiologie der Atembewegung, Handb. norm. path. Physiol. 2:70-127, 1925.

28. Vuilleumier, P.: Über ein Methode zur Messung des intraaveolären Druckes und der Strömungswiderstände in den Atemwegen des Menschen, Ztschr. klin. Med. 143:698-717, 1944.

29. Marshall, R.; McIlroy, M. B., and Christie, R. V.: Work of Breathing in Mitral Stenosis, Clin. Sc. 13:137-146 (Feb.) 1954.

30. McIlroy, M. B., and Christie, R. V.: Work of Breathing in Emphysema, Clin. Sc. 13:147-154 (Feb.) 1954.

31. Cherniack, R. M.: Physical Properties of the Lungs in Chronic Obstructive Pulmonary Emphysema, J. Clin. Invest. 35:394-404 (April) 1956.

32. Christie, R. V.: Dyspnœa in Relation to the Visco-Elastic Properties of the Lung, Proc. Roy. Soc. Med. 46:381-386 (May) 1953.

33. Mack, I.; Grossman, M., and Katz, L. N.: Effect of Pulmonary Vascular Congestion on the Distensibility of the Lungs, Am. J. Physiol. 150: 654-660 (Oct.) 1947.

34. Heyer, H. E.; Holman, J., and Shires, G. T.: Diminished Efficiency and Altered Dynamics of Respiration in Experimental Pulmonary Congestion, Am. Heart J. 35:463-479 (March) 1948.

35. Holaday, D. A., and Israel, J.: Alterations of the Work of Respiration During Anesthesia, Fed. Proc. 14:74-75 (March) 1955.

36. Nims, R. G.; Conner, E. H., and Comroe, J. H., Jr.: Compliance of the Human Thorax in Anesthetized Patients, J. Clin. Invest. 34:744-750 (May) 1955.

37. Wu, N.; Miller, W. F., and Luhn, N. R.: Studies of Breathing in Anesthesia, Anesthesiology 17:696-707 (Sept.-Oct.) 1956.

38. Mead, J.; Lindgren, I., and Gaensler, E. A.: Mechanical Properties of the Lungs in Emphysema, J. Clin. Invest. 34:1005-1016 (July) 1955.

39. Safar, P., and Bachman, L.: Compliance of the Lungs and Thorax in Dogs Under the Influence of Muscle Relaxants, Anesthesiology 17: 334-346 (March) 1956.

40. Cournand, A.; Richards, D. W., Jr.; Bader, R. A.; Bader, M. E., and Fishman, A. P.: Oxygen Cost of Breathing, Tr. A. Am. Physicians 67:162-173, 1954.

41. Riley, R. L., Jr.: Work of Breathing and Its Relation to Respiratory Acidosis, Editorial, Ann. Int. Med. 41:172-176 (July) 1954.

Clinical Aspects of Soft-Tissue Tumors

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Soft-tissue tumors or sarcomas of mesenchymal origin are a challenge to the therapeutic acumen of the surgeon. No tumor appears more innocuous while in the early stages of local growth, and none can be more virulently malignant when developed to the point where distant metastasis is manifest. These tumors are best treated by surgery. However, inadequate surgery at the time of the initial treatment is the principal reason for failure of cure and is the usual clinical history of a patient with sarcoma. With appropriate radical surgical technique, employing the method of incontinuity "en bloc" resection, the local lesion can be permanently eliminated with but few exceptions. If such surgery can be instituted as the initial treatment, it will circumvent distant metastasis in a higher percentage of cases than is now being achieved by repeated inadequate operative treatment. The chance for cure will be lost if one compromises on this principle of effective initial treatment.

Read at the 64th Annual Meeting of the Western Surgical Association, Cincinnati, Nov. 30, 1956.

Director and Surgeon-in-Chief, The University of Texas M. D. Anderson Hospital and Tumor Institute, and Professor of Surgery, The University of Texas Postgraduate School of Medicine (Dr. Clark); Associate Surgeon, The University of Texas M. D. Anderson Hospital and Tumor Institute, and Associate Professor of Surgery, The University of Texas Postgraduate School of Medicine (Dr. Martin); Chief, General Surgery Service, and Chairman, Department of Surgery, The University of Texas M. D. Anderson Hospital and Tumor Institute, and Professor of Surgery, The University of Texas Postgraduate School of Medicine (Dr. White); Assistant Pathologist, The University of Texas M. D. Anderson Hospital and Tumor Institute, and Assistant Professor of Pathology, The University of Texas Postgraduate School of Medicine (Dr. Old).

The present series of 122 cases depicts the natural history of soft-tissue tumors, presents a philosophy of treatment of extensive but carefully evaluated surgery, attempts to appraise the cause of failure of therapy, and discusses the value of palliation. The 122 patients discussed were treated at The University of Texas M. D. Anderson Hospital and Tumor Institute from 1944 to 1956. In each instance a microscopic diagnosis of soft-tissue sarcoma was obtained. Surgery was the treatment of choice and was performed with only one death.

Soft-tissue tumors are atypical growths arising from the connective tissue. They arise from the nonepithelial mesenchymal structures, such as fascia, muscles, adipose tissue, and synovial membranes. These tumors may be either benign or malignant. The benign lesions are usually important only in differentiating them from the malignant sarcomas.

It is generally known that mesenchymal structures are found throughout the body and in all the organs of the body. Therefore, sarcomas may be found anywhere in the body and its viscera. Because the sarcomas arising in the viscera are so very rare, and therefore relatively unimportant and also present a different problem in treatment, we will concern ourselves only with those arising in the connective tissues of the head, neck, trunk, extremities, and retroperitoneal areas. Thus, we will consider mainly the fibrosarcomas, liposarcomas, rhabdomyosarcomas, synovial sarcomas, and angiosarcomas. At The University of Texas M. D. Anderson Hospital and Tumor Institute, this group consists of only approximately 0.88% of all the tumors seen. Figure 1 shows a simpli-

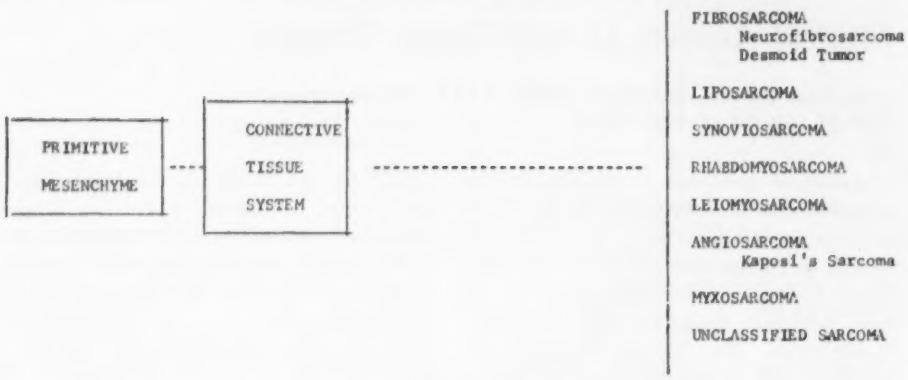


Figure 1

fied diagram of the classification of soft-tissue sarcomas.

Nature of Soft-Tissue Sarcomas

The etiology of these tumors is still unknown. Trauma, often connected with the first symptom by the patient, is believed in no way to contribute to the etiology. Twelve of our cases gave a history of possible trauma preceding their knowledge of the presence of a tumor. Irradiation treatment given for benign conditions is recognized as an important factor in the production of malignant epithelial tumors, and, although it has been established that true sarcomas may develop in tissue damaged by irradiation, the incidence is small. The interval between radiotherapy and tumor formation varies from 1½ to 20 years but is more commonly about 5 years.

A "lump" or swelling anywhere in the body is usually the presenting symptom. In most instances these tumors are discovered by accident or because of symptoms resulting from encroachment upon nerves or vital organs. These tumors may be hard or soft and may be painful, although pain, as a rule, is not the initial symptom. The lesion may attain considerable size before pain and disability result. In the later stages pain is invariably constant and is aggravated by motion. If untreated, soft-tissue sarcoma may grow to enormous size and sometimes break through the skin and ulcerate. The resulting fungating hemorrhagic mass may become infected. Hemorrhage from exposed tumor surfaces usually causes secondary anemia, and in the later stages infection may cause severe weight loss and high fever. Coughing and dyspnea frequently occur at this point as pulmonary metastasis becomes evident.

These tumors are no respectors of age. They can be found in the young as well as the elderly patient, with the peak incidence falling in the 30- to 60-year-old range. The sex distribution is almost equal, as shown in Table 1.

As stated previously, these tumors may be found wherever tissues derived from mesoderm are located. However, they are seen much more frequently on the extremities and especially the lower extremity (Fig. 2). This is fortunate, for tumors

TABLE 1.—*Age and Sex Distribution*

Age	Male	Female	Grand Total
0-9	5	5	10
10-19	5	1	6
20-29	5	9	14
30-39	9	13	22
40-49	17	11	28
50-59	10	7	17
60-69	9	7	16
70-79	3	4	7
80-89	2	--	2
Totals	65	57	122

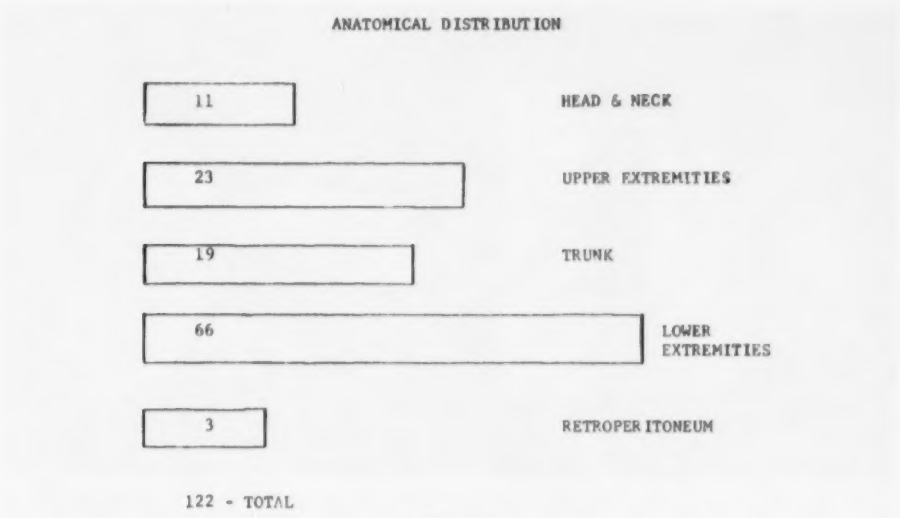


Figure 2

in the extremities can more adequately be completely excised than those on the body and in the head and neck areas.

The consistency of soft-tissue sarcomas ranges from firm, solid, smooth lesions, such as the fibrosarcomas, to soft, lobulated lesions, such as the liposarcomas and those tumors with a high degree of myxomatous element. They may be small and solid, or large with a necrotic center. All these lesions, with the exception of the low-grade fibrosarcomas and liposarcomas, are quite vascular, especially the rhabdomyosarcomas and angiosarcomas.

At the surface of these tumors the cells tend to "layer out" in a series of flat planes parallel to the surface. This "layering-out" is due to the internal pressures of the tumor and represents planes of weakness which are the natural lines of cleavage. In addition to this simple type of boundary between tumor and normal tissue, a zone incorporating fibrous elements from the surrounding tissues may form around part or all of the tumor nodule. This layer has been termed a "pseudocapsule," since in many instances it has the aspects of a true capsule which may surround a benign tumor. This pseudocapsule varies in density in different areas and has many potential planes of cleavage. Further, the pseudocapsule is often discontinuous, and cleavage planes either within or without may continue into the natural planes formed by the "layering-out" process described above. Because of these continuous planes of cleavage, these tumors can usually be enucleated with the impression that the tumor has been easily and completely removed from the patient's body. This is not the case, for viable tumor almost always remains in the patient's body at some points around the plane of enucleation, since the cleavage planes "wander" from the inside to the outside of pseudocapsule during the process of enucleation.

Two gross photographs (Fig. 3) and four photomicrographs (Figs. 4 to 7) have been prepared to illustrate certain aspects of the nature of a pseudocapsule which surrounds a subcutaneous fibrosarcoma. All photographs are from the same tumor nodule.

The gross photographs (Fig. 3) are designed to show the planes of cleavage around a tough pseudocapsule. These are "before and after" studies of a single cross section of the tumor nodule, and the point *X* is used to designate the free end of the pseudocapsule which has been stripped. In Figure 3*A* the arrow is directed to a natural

Fig. 3.—*A*, gross photograph of half of transected tumor nodule. Point *X* indicates plane of cleavage between tumor and pseudocapsule, which has been started. Arrow indicates natural cleavage plane outside pseudocapsule. *B*, gross photograph of same tumor nodule after partial stripping of pseudocapsule from tumor. Arrows indicate tumor fragments and strands adherent to inner surface of pseudocapsule.

cleavage plane outside the pseudocapsule. Figure 3*B* shows the stripped pseudocapsule with the natural cleavage plane between the pseudocapsule and the tumor disrupted. The left-hand arrow indicates several small fragments of tumor adherent to the inner surface of the pseudocapsule, and the right-hand arrow shows strands of fibrillar tumor tissue in the process of rupturing at the farthest point of cleavage. These photographs illustrate why any part of the pseudocapsule which remains in the patient's body may be the source of recurrent tumor.

The photomicrographs show some of the aspects of the pseudocapsule. Figure 4 shows the condensation of collagen-containing tumor cells which is the intact pseudocapsule (designated *PSC*). Figure 5 shows the natural cleavage plane on the inner (or tumor) side of the pseudocapsule; note that the cleavage is beginning to wander away from the tumor. Figure 6 shows a natural cleavage plane dividing the inner and outer halves of the pseudocapsule. Figure 7 shows a less collagenized area of the pseudocapsule, any layer of which is a potential plane of cleavage. The pseudocapsule clearly contains tumor cells, but, more important, appositional growth of tumor can be seen outside the pseudocapsule (*T2*).

Metastasis from sarcomatous lesions in these patients is usually by way of the blood stream and most frequently first becomes evident in the lungs. The liver and other organs of the body may also become sites of metastasis. The lymph nodes become involved only rarely in the fibrosarcoma group but not infrequently in cases of synovial sarcoma and liposarcoma and occasionally in cases of rhabdomyosarcoma and angiosarcoma. Six cases out of our group of 122 cases had proved lymph-node metastasis. The average time, in those cases developing generalized disease, from proved diagnosis to proved metastasis was 13.7 months. The average time from the diagnosis of metastasis until death was 8.4 months. The longest interval was 25 months.

Treatment

Before any form of treatment can be instituted, a proved histological diagnosis must be made. This diagnosis is made by obtaining a specimen for biopsy, either by excision of the mass, by incision, or by

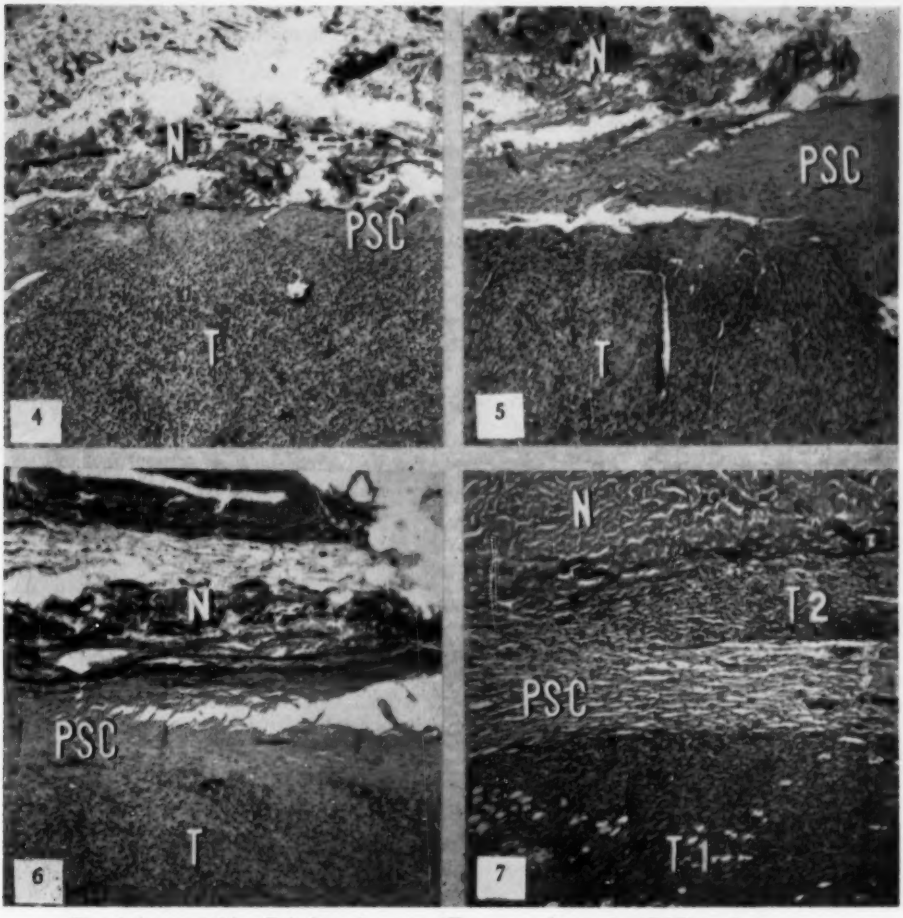


Fig. 4 (upper left).—Relation of tumor (*T*) to pseudocapsule (*PSC*) and normal tissue (*N*). Note that tumor and pseudocapsule are continuous. Hematoxylin and eosin; × 50.

Fig. 5 (upper right).—Natural cleavage plane between tumor (*T*) and pseudocapsule (*PSC*). Note apex of cleavage plane beginning to "wander" into pseudocapsule. A natural cleavage plane outside pseudocapsule may also be seen. Hematoxylin and eosin; × 50.

Fig. 6 (lower left).—Natural cleavage plane within pseudocapsule (*PSC*), dividing it into inner and outer halves. Hematoxylin and eosin; × 50.

Fig. 7 (lower right).—Pseudocapsule (*PSC*) showing less collagen condensation than seen in Figures 5, 6, and 7. Main tumor mass (*T1*). Note tumor growth (*T2*) outside pseudocapsule. Hematoxylin and eosin; × 50.

aspiration. We do not like to rely, as a rule, upon a frozen-section diagnosis because of the radical nature of many of our procedures.

It is obvious, after reviewing the nature of the pseudocapsule about these tumors, that they must be widely excised. This may require for superficial lesions a wide excision with the underlying fascia, followed frequently by a split-thickness skin graft, or for the deeper lesions a wide excision to include the muscle bundles involved. This means removing the muscle bundles at their origins and insertions. The drawings in Figures 8, 9, and 10 illustrate cases in which this type of procedure was used.

Case 1.—This patient is a Negro youth, aged 19 years. In 1949 he first noticed a mass on the lateral aspect of the right upper arm. A local excision was done in 1950 and again in 1951. The

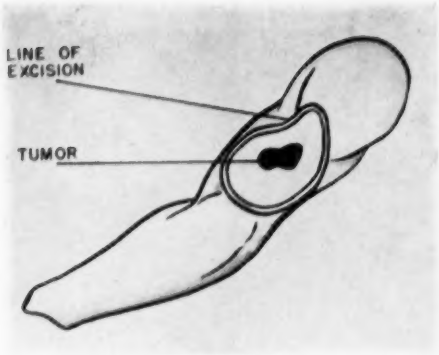


Figure 8—Case 1

diagnosis of fibrosarcoma was made after the latter excision. In October, 1956, we did the wide excision shown in Figure 8, including the underlying fascia. A split-thickness skin graft was applied.

CASE 2.—This patient was only 3 years old when he was first seen in the clinic, in 1951. At that time he had a mass on the posterior aspect of the right shoulder. This had previously been locally excised, and the diagnosis of fibrosarcoma, Grade III, was made. An intrascapulothoracic amputation was refused; therefore, a wide excision taking the entire supraspinatus muscle and the upper half of the scapula was performed (Fig. 9). The patient is still living with no evidence of local recurrence or pulmonary metastasis.

CASE 3.—This man, at the age of 56, developed pain in the left midlateral thigh. A mass soon became noticeable in this area. Two months later, after an amputation had been refused, a wide radical excision removing the vastus lateralis muscle and the biceps femoris muscles from their origins to their insertions was performed (Fig. 10). The patient died two years later, but there had been no local recurrence.

Amputations are reserved for the larger, deeper lesions in cases in which a wide radical excision cannot be done because of the uselessness of the remaining limb, or in which it would be impossible to adequately remove the tumor. Example cases are illustrated in Figures 11 and 12.

CASE 4.—This case is that of a 38-year-old white man who in 1955 had a nodule removed under local anesthesia in a physician's office. The nodule had been present for almost a year. It was necessary to send the slide away for diagnosis. Two weeks later the diagnosis of synovial sarcoma was made. The patient was admitted to The University of Texas M. D. Anderson Hospital and Tumor Institute in August, 1955. A midthigh amputation was performed (Fig. 11). In May, 1956, routine x-rays showed rib and lung metastases. The patient soon developed other bony lesions that were very painful. X-ray therapy has controlled the pain quite well.

CASE 5.—This 22-year-old white man first noticed a mass behind his left knee in 1953. It remained unchanged until June, 1955. It was then partially excised, and the diagnosis of fibrosarcoma, Grade III, was made. On June 15, 1955, we per-

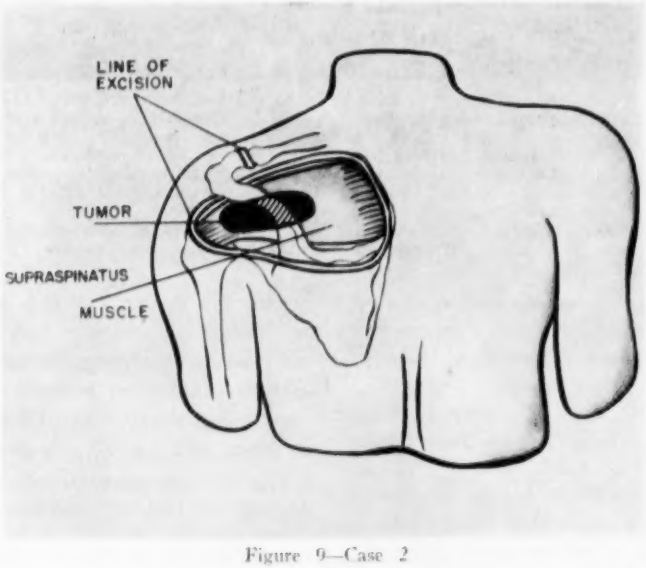


Figure 9—Case 2

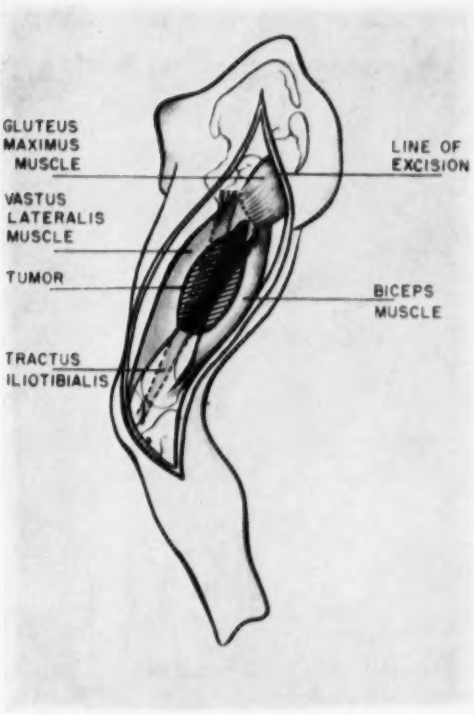


Figure 10—Case 3

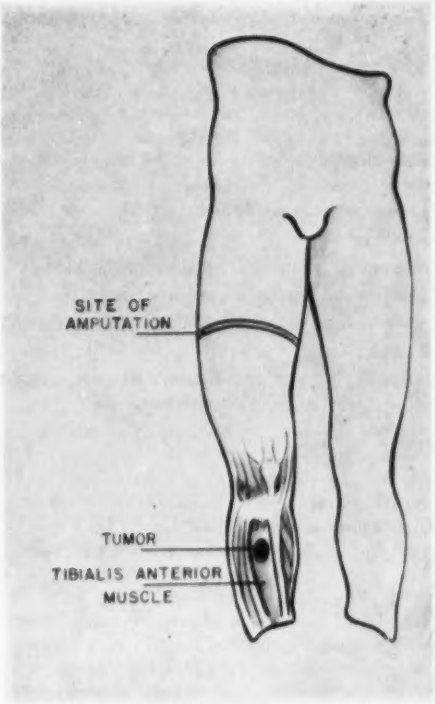


Figure 11—Case 4

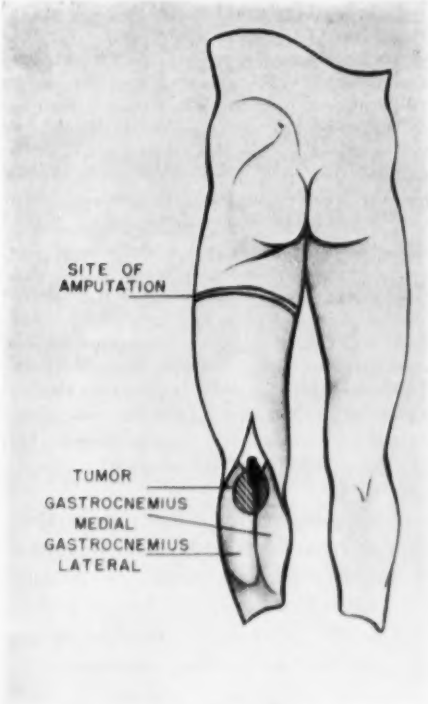


Figure 12—Case 5

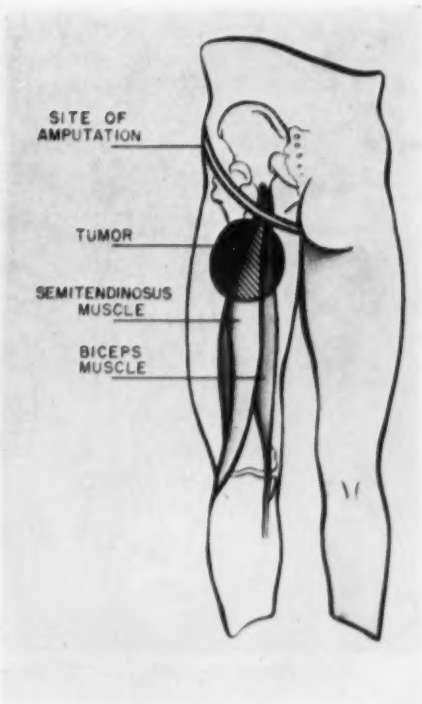


Figure 13—Case 6

formed a midthigh amputation (Fig. 12). In July, 1956, routine chest x-rays revealed bilateral pulmonary metastasis, but clinically the patient was doing well. On Oct. 18, 1956, he was last seen in the clinic and appeared well, in spite of the increase in size of the pulmonary metastasis.

Disarticulations are done for large, deep lesions of the thigh in cases in which radical excision of muscle bundles is impossible. Shoulder disarticulations are not done because of the difficulty in clearing the muscles at their origins. Therefore, for large lesions above the elbow intrascapulothoracic amputations are preferred.

CASE 6.—This is a case of a 65-year-old white woman who in November, 1955, developed pain and swelling in the right posterior thigh. The patient was admitted in January, 1956. Following the diagnosis of fibrosarcoma, a right hip disarticulation and an iliac-node dissection were performed (Fig. 14). A large mass, 15 cm. in diameter, was found deep to the biceps femoris muscle. By July, 1956, the patient developed multiple pulmonary metastasis and died.

CASE 7.—This 56-year-old white woman first noticed the appearance of a mass in the anteromedial aspect of the right thigh. It increased in size rapidly. Six months later she sought medical advice. A biopsy was done, and the mass was diagnosed as rhabdomyosarcoma, Grade III. A right iliac-node dissection and a hip disarticulation were performed (Fig. 14). In November, 1956, five months later, there was no evidence of local or generalized disease.

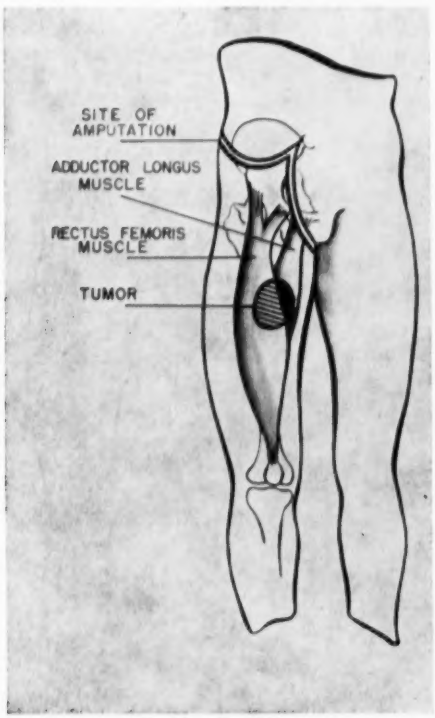


Figure 14—Case 7

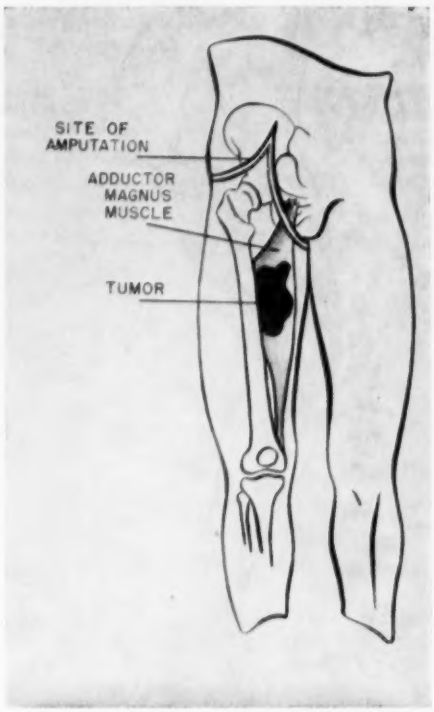


Figure 15—Case 8

CASE 8.—This 24-year-old white man in July, 1956, developed a nontender mass in the inner upper aspect of the right thigh. He received intensive physical therapy before a diagnosis was made, following biopsy, of rhabdomyosarcoma, Grade III. In August, 1956, he was admitted to The University of Texas M. D. Anderson Hospital and Tumor Institute, and a right iliac-node dissection and hip disarticulation were performed (Fig. 15). There was no clinical evidence of recurrence in November, 1956.

Intrascapulothoracic and hemipelvectomy amputations are done only if the lesion and its involved structure cannot be removed with lesser procedures. The lesions in these cases usually involves the shoulder or hip joints and their surrounding structures.

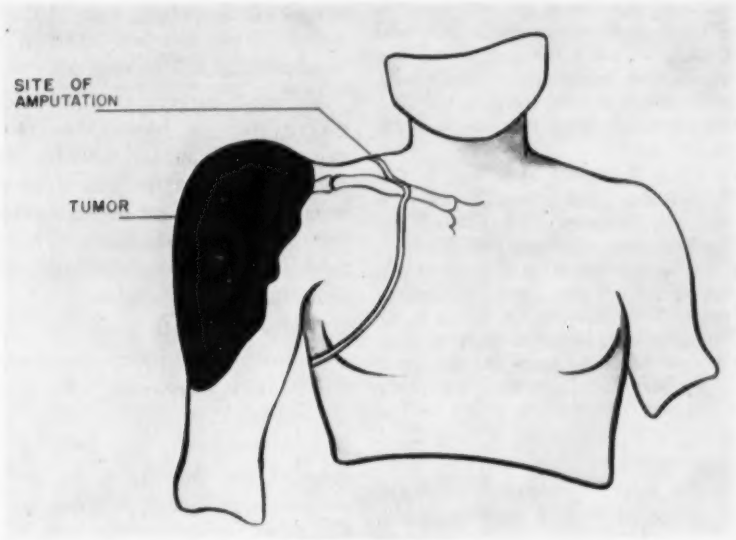


Figure 16—Case 9

CASE 9.—This case is that of a one-year-old white girl. At the age of 2 weeks, her mother noted that the right shoulder appeared larger than the left. By the age of 5 months, it became greatly enlarged, but little was done until the child was referred for treatment. A biopsy was performed, and a diagnosis of fibrosarcoma, Grade III, was made. Chest x-rays were negative for metastasis. An intrascapulothoracic amputation was performed (Fig. 16), and the patient did well until five months later, at which time she died, death being due to pulmonary metastasis.

CASE 10.—This 19-year-old white youth developed pain and swelling of the right wrist in 1951. In August, 1952, a mass was excised and diagnosed as sarcoma. Later that month the patient came to us with a mass in the right axilla, which on biopsy proved to be synovial sarcoma. A right intrascapulothoracic amputation was then performed (Fig. 17). No other positive lymph

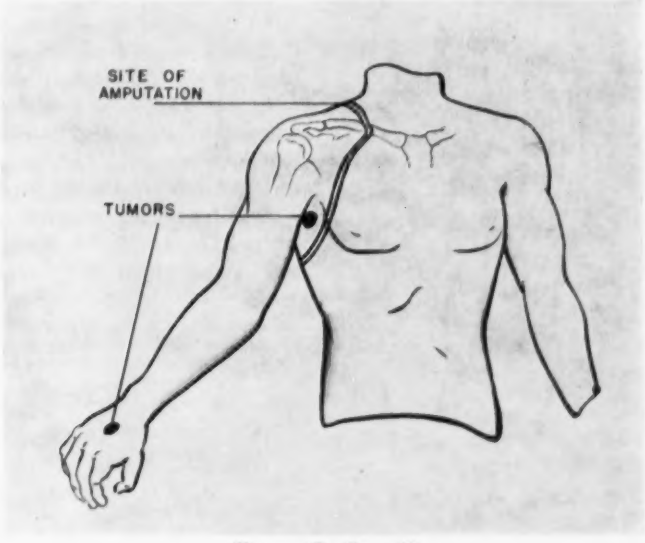


Figure 17—Case 10

nodes were found, but tumor was still noted in the wrist. The patient did exceedingly well until September, 1956, at which time he developed a serosanguineous fluid in the right chest cavity. No malignant cells have been found in the fluid. The patient, clinically, still appears to be doing well.

CASE 11.—This 30-year-old white man in October, 1951, developed a small "knot" in the right inguinal area. In December, 1951, a blood clot was said to have been removed from this area. The area was reexplored in May, 1952, and a fibrosarcoma, Grade III, was found. The patient was admitted to The University of Texas M. D. Anderson Hospital and Tumor Institute in May, 1952, and a right hemipelvectomy was performed (Fig. 18). By March, 1953, multiple pulmonary metastases had developed, and the patient died in August, 1953.

X-ray therapy and chemotherapy have little to offer in the treatment of these sarcomas, except in cases having multicentric foci, such as Kaposi's sarcoma. In these cases x-ray therapy is the treatment of choice. In cases in which bony metastasis has occurred, causing a great deal of pain, x-ray therapy has been used to advantage in alleviating this pain.

Palliative surgery is often necessary to relieve pain or hemorrhage in incurable cases. Indication for palliative surgery is the certainty that the procedure will be of benefit to the patient by decreasing discomfort or reducing disability. The procedure most frequently employed for palliation is some form of amputation.

One should not leave the subject of treatment without mentioning pneumonectomies and lobectomies for pulmonary metastasis. These procedures in certain cases of carcinoma have been encouraging; however, in patients with sarcoma lung metastasis is usually multiple and there is dissemination throughout both lung fields. Therefore, we have abandoned these procedures in cases of sarcoma.

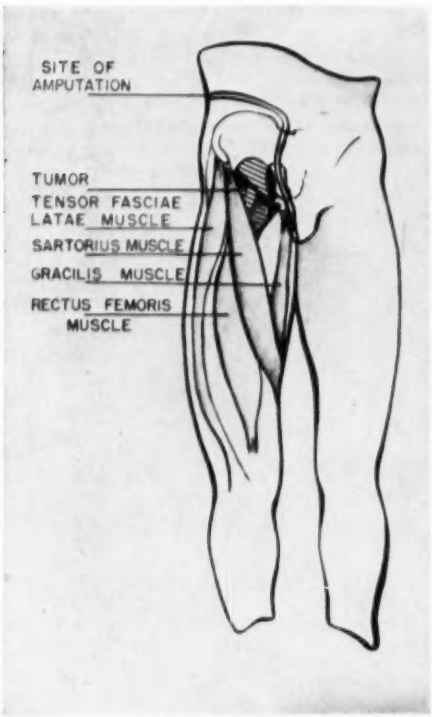


Figure 18—Case 11

Results and Conclusions

We have found that, unlike patients with "lumps" in their breasts, these patients frequently do not seek medical advice until late. In our group of cases the average time between the awareness of the first symptoms and treatment was 16.6 months. Even with this delay it is interesting to note that the great majority of cases at the time of diagnosis had localized disease. Of our 122 cases, 83.7% had localized disease when diagnosed. It is also interesting to note that approximately 82% of our cases had had previous treatment, usually local excision, before being referred to the University of Texas M. D. Anderson Hospital and Tumor Institute. In evaluating our

TABLE 2.—*Local Recurrence Rate of Sarcomas of Soft Tissues*

	Total Cases	One Recurrence	Multiple Recurrence	Total Recurrences
Local excision	85	34	21	55
Local excision followed by radical surgery	50	5	--	5
Radial surgery only	21	2	--	2
No treatment (inoperable or refused surgery)	16	--	--	--

TABLE 3.—*Sarcomas of the Soft Tissues*

Year of Diagnosis	Total Cases	Total Traced	Cases Alive Year of Diagnosis	1 Year	2	3	4	5	6	7	8	9	10	11	12	13
1938	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
1942	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
1944	2	2	1	..	..	..	..	..	..	..	..	..	..	..		
1945	2	2	1	1	1	1	1	1	1	1	..	..	..			
1946	2	2	2	1	1	1	..	..	..	..	..	..				
1947	2	2	2	1	1	1	1	1	1	1	1					
1948	10	10	10	9	9	5	4	4	4	2						
1949	7	7	6	4	4	4	3	2	2							
1950	14	14	14	11	9	9	9	8								
1951	10	10	8	7	6	4	4									
1952	23	23	22	17	16	12										
1953	15	15	13	12	10											
1954	19	19	19	16												
1955	7	7	7													
1956	7	7	*													

* Year not over.

treatment in these cases, Table 2 sums up clearly the necessity or wisdom of doing wide radical excisions for sarcomas of the soft tissues.

It should be noted that, in 85 cases of local excisions, 34 cases had one recurrence and 21 cases had multiple recurrences, or a total of 55 local recurrences out of 85 cases. In those treated with wide radical excision after they had had a local excision, only 5 cases out of 50 had local recurrence. In 21 cases that were primarily treated with radical surgery, there were only 2 with local recurrence. Of the seven failures after radical surgery, two were in cases of liposarcomas in the retroperitoneum, four in the head and neck area where adequate radical excision is often impossible, and one of the chest wall where, again, adequate wide excision was impossible. It seems, therefore, from the above results that one should be able in most instances to control the local lesion. As to the control of the metastatic spread, this still remains a challenge.

The over-all survival rate in terms of five-year survival for all the soft-tissue sarcomas, irrespective of classification or grade, in our series is 41%. The portion of Table 3 set in bold-face type represents those cases diagnosed and treated here at The University of Texas M. D. Anderson Hospital and Tumor Institute, from its beginning in 1944 to 1950, who have survived five years.

Summary

A series of 122 cases of soft-tissue sarcomas is presented.

The natural history of these tumors is outlined, with emphasis being placed upon the pseudocapsule.

With the nature of the pseudocapsule in mind, we have outlined the treatment used at The University of Texas M. D. Anderson Hospital and Tumor Institute for cases of soft-tissue sarcomas, favoring wide radical excisions.

Out of 85 cases having local excision, there were 55 cases of local recurrence, as compared with only 7 local recurrences out of 71 cases following wide radical excision.

Thirty-nine of the 122 patients in the series have been treated more than five years ago. Of that group, 16 survived five years or longer since the initial treatment by us. This is a 41% five-year survival rate, regardless of classification or grade.

Soft-tissue tumors can be cured locally in practically all instances if adequate initial surgery is well conceived and well executed. Those in the abdominal cavity furnish the chief exception to this statement.

Distant metastasis possibly can be prevented in a higher number of patients if their initial treatment is adequate.

The University of Texas M. D. Anderson Hospital and Tumor Institute, Texas Medical Center (25) (Dr. Clark)

DISCUSSION

DR. JOHN W. STEWART, St. Louis: In discussing this paper, I would just like to add an occasion of soft-tissue tumor recently encountered.

A 75-year-old white woman was first seen on Sept. 22, 1954. She had a radical breast amputation, right, five years previously (1949) with persistent edema of the right arm since the operation.

In January, 1954, a bluish discoloration appeared on the anterior surface of the right arm. In June, 1954, the lesion ulcerated with much bleeding from its surface. Other lesions appeared later and coalesced. Hemoglobin was 11.4 gm. X-rays of the chest showed no parenchymatous pathology in either lung field. No evidence of metastatic malignancy in skull, vertebrae, or long bones.

A shoulder girdle amputation was done on Oct. 6, 1954.

Pathological diagnosis: Endothelial sarcoma of lymphatic origin (N. B.).

This tumor is similar to the tumors described by Fred W. Stewart and Norman Treves in *Cancer* 1:64-81, 1948 (Dr. Stanton, pathologist).

There was local recurrence in the scar on Nov. 29, 1954.

The patient died of lung metastases in January, 1955, a year after the lesion on arm appeared.

[Slide] Here is the appearance of the lesion in this edematous arm on admission to the hospital. Lymphedema following radical breast surgery. The patient was operated on elsewhere.

[Slide] Another view; the mark is where we propose to make our skin incision.

[Slide] A posterior view of the same patient.

[Slide] This is the shoulder girdle amputation done in October.

[Slide] Next is a lateral view immediately after the operation.

Fred W. Stewart and Norman Treves (*Cancer* 1:64-81, 1948) reported six cases of lymphangiosarcoma in postmastectomy lymphedema of the arm.

After an interval of years in a post-radical-mammectomy lymphedematous arm, a purplish-red, subdermal, slightly raised macular or polypoid lesion appears. The lesion occurs as a solitary tumor followed by similar satellite areas which become confluent. Bullous areas appear.

The larger lesions appear almost as a papillomatosis growth covered by a shiny atrophied epithelium that has a tendency to ulcerate and discharge a serous or serosanguineous exudate. With increase in size the largest lesions become cystic and finally necrose, leaving a central cystic cavity.

Clinically, these dermal tumors do not resemble the cutaneous nodules of recurrent mammary cancer. In no instances have the reported cases shown evidence of local or metastatic carcinoma.

The tumor remains aggressive until radical amputation of the arm or the shoulder girdle interferes with its growth, or the patient dies with metastases. In the experience of Stewart and Treves x-ray treatment elicits very little response.

Cases of lymphangiosarcoma in postmastectomy lymphedema have also been reported by Ferraro (*Cancer* 3:511-514, 1950 [claimed to be the 11th case reported]), Cruse, Fisher, and Usher (*Surgery* 30:565-569, 1951), and Froio and Kirkland (*Ann. Surg.* 135:421-425, 1952).

Hidrocystoma tuberosum multiplex of epithelial origin was reported by Ewing in "Neoplastic Diseases," 1940, p. 371. Two of these cases were confused with Kaposi's disease, but later studies revealed their true diagnosis. Also, it should be noted that edema follows the onset in Kaposi's disease.

BIBLIOGRAPHY

Ackerman, L. V., and del Regato, J. A.: Cancer, Ed. 2, St. Louis, The C. V. Mosby Company, 1954, p. 1069.

Burdick, D.: Treatment of Soft Tissue Tumors, New York J. Med. 56:722 (March 1) 1956.

Cade, S.: Soft Tissue Tumours: Their Natural History and Treatment, Proc. Roy. Soc. Med. 44:19 (Jan.) 1951.

Haagensen, C. D., and Stout, A. P.: Synovial Sarcoma, Ann. Surg. 120:826 (Dec.) 1944.

Lieberman, Z., and Ackerman, L. V.: Principles in Management of Soft Tissue Sarcomas, Surgery 35:350 (March) 1954.

Pack, G. T.: End Results in the Treatment of Sarcomata of the Soft Somatic Tissues, J. Bone & Joint Surg. 36-A:241 (April) 1954.

Pack, G. T., and Ariel, I. M.: Sarcomas of the Soft Somatic Tissues in Infants and Children, Surg. Gynec. & Obst. 98:675 (June) 1954.

Pack, G. T., and Ariel, I. M.: A Half Century of Effort to Control Cancer, Internat. Abstr. Surg. 100:309-352, 425-457, and 526-552, 1955; in Surg. Gynec. & Obst., April-June, 1955.

Soule, E. H.; Ghormley, R. K., and Bulbulian, A. H.: Primary Tumors of the Soft Tissues of the Extremities Exclusive of Epithelial Tumors, A. M. A. Arch. Surg. 70:462 (March) 1955.

Stout, A. P.: Rhabdomyosarcoma of the Skeletal Muscles, Ann. Surg. 123:447 (March) 1946.

Stout, A. P.: Fibrosarcoma, Cancer 1:30 (May) 1948.

Sarcoma of Soft Parts, Cancer Bull. 2:99 (Sept.-Oct.) 1950.

Pancreaticoduodenectomy for Chronic Relapsing Pancreatitis

Metabolic Defects Created by Total and Subtotal Ablations

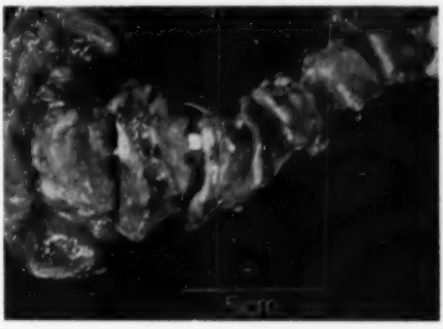
PAUL H. JORDAN Jr., M.D., and MORTON I. GROSSMAN, M.D., Ph.D., Los Angeles

Although von Mering and Minkowski were successful in removing the pancreas from the dog in 1889, it was almost 50 years before a similar procedure was accomplished in man. In 1935 Whipple[16] performed the first subtotal pancreaticoduodenectomy, and in 1944 Priestley[12] performed the first successful total pancreatectomy. During the two decades since Whipple's operation was originally described, pancreatectomy has been utilized with increasing frequency in the treatment of an array of benign and malignant diseases.

The incidence of unsatisfactory results that are obtained in the treatment of chronic relapsing pancreatitis with indirect surgical procedures has stimulated interest in the treatment of this disease by more direct operative techniques, including resection of the pancreas.[2] A similar dissatisfaction with the results obtained by less radical but more conventional methods of treatment also prompted us to evaluate pancreaticoduodenectomy in selected cases that are characterized by far-advanced architectural changes of the head and body of the pancreas or of the entire gland. We have not advocated this procedure when the pathological process was limited to the tail of the pancreas. Because it appears that architectural destruction of the pancreas most frequently proceeds in a caudal direction from the head of the gland, we have suggested that the tail of the pancreas should not be resected, even though it may appear to be grossly involved in the inflammatory process.

The factors which are helpful in selecting cases for resection are (1) the characteristic history of recurrent attacks of abdominal pain; (2) loss of weight; (3) steatorrhea; (4) roentgenographic evidence of pancreatic calcification, and (5) a failure of the pancreas to respond to secretin. Patients fulfilling all or most of these criteria and who are not narcotic addicts are suitable for subtotal pancreaticoduodenectomy. If, in

Fig. 1.—The pancreas from Patient E. M., depicts the marked architectural changes predicted by preoperative studies. The gland was hard, fibrotic, and contracted. The main pancreatic duct was dilated and impacted throughout its length with concretions.



This work was aided in part by a grant from the VioBin Corp., Monticello, Ill.

Read at the 64th Annual Meeting of the Western Surgical Association, Cincinnati, Nov. 30, 1956.

From the Departments of Surgery and Medicine, Wadsworth General Hospital, Veterans' Administration Center, and University of California Medical Center. Assistant Chief of Surgery, Veterans' Administration Center and Assistant Clinical Professor of Surgery, University of California Medical Center (Dr. Jordan); Chief of Gastroenterology, Veterans' Administration Center and Associate Clinical Professor of Medicine, University of California Medical Center (Dr. Grossman).

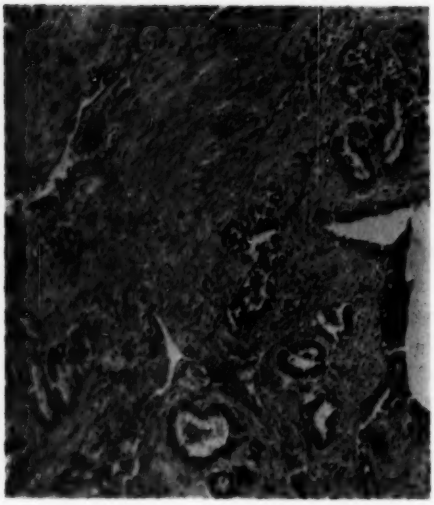


Fig. 2.—A photomicrograph of the pancreas from Patient E. M. demonstrates marked fibrosis, inflammation, ductal dilatation, and calcium deposits in the remaining acinar tissue.

addition, the patient is also diabetic, requiring insulin, the indications for total pancreatectomy are more compelling. Utilizing these criteria, we performed five subtotal and three total pancreaticoduodenectomies. The results were described in an earlier report.[8] Subsequently, an additional total pancreatectomy was performed. The degree of architectural involvement in this case is clearly seen in the gross specimen (Fig. 1) and the photomicrograph of a representative area (Fig. 2).

In terms of the large number of cases of pancreatitis, it is recognized that treatment of chronic relapsing pancreatitis by resection is a therapeutic measure of limited applicability. In addition, a perceptible degree of resistance to this form of therapy is encountered because of the fear of producing severe metabolic alterations. It is our opinion that, if the clinical evidence for severe architectural destruction of the pancreas is required as the indication for operation, the postoperative metabolic defects should not be significantly greater than the preoperative ones.

Several previous reports by others have dealt with the metabolic changes associated with pancreatectomy.[3-5,13,15,17] Since no investigator's total experience in this field is extensive, these reports have necessarily dealt with only a few cases. For this reason, we studied six of our patients (three total and three subtotal pancreaticoduodenectomies) to obtain additional information that might contribute to the understanding of the physiological alterations which follow total and subtotal ablation of the pancreas in man.

Procedure

Subjects.—Total pancreatectomy was performed upon three male patients, S. D., L. R., and E. M., aged 39, 34, and 47 years, respectively. These patients were subjected to metabolic studies 12, 10, and 2 months, respectively, after operation. Subtotal pancreaticoduodenectomy was performed upon three additional male patients, C. C., L. F., and V. H., aged 63, 34, and 38 years, respectively. Metabolic studies were made on these patients 5.5 years, 20 months, and 16 months, respectively, following operation.

Conventional Absorption Studies.—Patients V. H., S. D., and E. M. were admitted to the research metabolic ward. Preliminary trial periods were run to accustom the patients to the routine of making metabolic collections. During the trial periods the patients selected diets which were to their satisfaction in order that constant caloric, nitrogen, and fat intakes could be maintained throughout the study. The study of each patient consisted of four consecutive five-day metabolic periods, except for Patient S. D., whose second period consisted of six days. Sample diets from each period were analyzed for their nitrogen and fat content. A portion of Patient S. D.'s diet of day 5, period 4, was the only food rejected by these patients. The uneaten food was analyzed, and the nitrogen and fat content deducted from the amount of these substances in the diet. Six grams of pancreatin (Viokase) was administered daily to Patients V. H. and E. M. during Periods 1 and 2 but was discontinued during Periods 3 and 4. Patient S. D. received 6 gm. of Viokase daily during Periods 3 and 4 but none during Periods 1 and 2. During these studies the urine from patients with total pancreatectomy was tested for sugar and acetone four times a day; diabetes was controlled with isophane (NPH) insulin, supplemented with regular insulin according to the degree of glycosuria.

The beginning and the end of the stool collection for each period were marked with carmine. The stool collection for each period was analyzed for total lipids by a standard gravimetric method and for nitrogen by the micro-Kjeldahl method.

Nitrogen determinations were made on daily 24-hour urine collections, as well as the urine pool for each period by the macro-Kjeldahl method.

Radioactive Absorption Studies.—The absorption of fat, fatty acid, and protein was further investigated by studies utilizing I^{135}-labeled triolein and oleic acid and radioiodinated (I^{131}) serum albumin (human) (RISA), respectively. The methods employed for the study of each of these substances were essentially the same. One hundred microcuries of the material to be tested was administered orally at 8 a. m. after a 12-hour fast. Stools were collected for 72 hours, weighed, and then homogenized. Two milliliters of blood was drawn two, four, and six hours after the administration of RISA and three, six, and nine hours after the administration of triolein or oleic acid. The blood samples and aliquots of the stools in duplicate were assayed for their radioactivity in a scintillation crystal well counter. The radioactivity of the stool and blood samples was expressed as the per cent of the administered radioactivity in 1 ml. of blood and in the total stool collection. In some patients the absorption of triolein and RISA was evaluated with and without the concomitant administration of Viokase. No other specific medications were employed during these studies except insulin, which was administered to those patients requiring it.

Radioactive iron was utilized in studies of the gastrointestinal absorption of iron. Ten microcuries of Fe^{59} in the form of ferrous citrate was administered orally. After the administration of iron, all stools were collected for five days, and blood was drawn once a week for three to four weeks. The blood samples and aliquots of the stool were analyzed for radioactivity in a scintillation crystal well counter. The total blood volume was determined by the Evans blue technique. With use of the measured radioactivity of the blood samples and the estimated total blood volume, the total radioactive Fe^{59} of the blood was calculated and expressed as a per cent of the ingested material. The blood sample with the highest radioactivity represented the maximum absorption of iron by the patient. The total radioactivity of the stool was determined from the radioactivity of the sample and was expressed as a per cent of the total dose of ingested material.

Pancreatin.—The preparation of pancreatin used in these studies was Viokase, which is produced from raw pancreas by azeotropic desiccation rather than by methods generally employed. Viokase is effective in smaller doses than are other pancreatic substitution products and is not accompanied by the untoward digestive symptoms usually encountered with large doses of other types of pancreatin. Viokase has a high enzymatic content of increased stability, which is effective without an enteric coat. The high enzymatic activity of this preparation is related to the fact that it is desiccated and defatted whole pancreas rather than an extract.

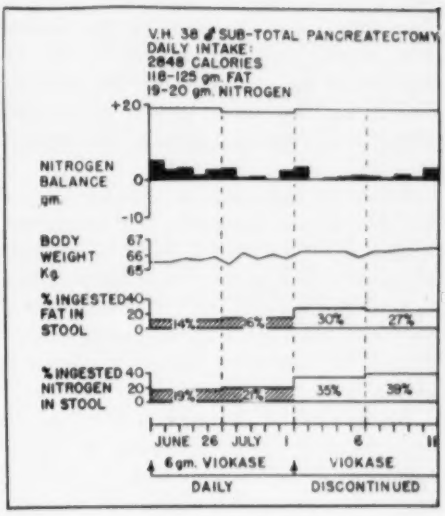


Fig. 3.—Metabolic chart.

Results

Conventional Absorption Studies.—The graphic representation of the data obtained from the study of Patient V. H. (subtotal pancreatectomy) is seen in Figure 3. His daily diet consisted of 2848 Cal., 19.4 to 19.9 gm. of nitrogen, and 118.7 to 128.1 gm. of fat. The mean daily urinary nitrogen output for the four periods was 12.5, 13.6, 11.7, and 10.7 gm., while the mean daily stool nitrogen for these periods was 3.8, 4.0, 6.7, and 7.6 gm., respectively. In spite of the large fecal nitrogen losses in all periods, the patient remained in positive nitrogen balance throughout the study, although the degree of nitrogen retention was greater when Viokase was administered. During those two periods 19% and 21% of the ingested nitrogen appeared in the feces, as compared with 35% and 39% during the two periods when Viokase was withheld.

A derangement in fat absorption was also present throughout the study, and it likewise

was greatest when Viokase was withheld. The mean daily content of fat in the feces during the four periods was 17, 21, 34, and 34 gm., respectively. The fecal fat during each of these periods represented 14%, 16%, 30%, and 27% of the ingested fat.

Although this patient maintains good health and a satisfactory, but subnormal, weight, it is clear that a defect in digestion is present which prevents maximum absorption of protein and fat. The regimen of pancreatic substitution therapy employed improved the defect but did not restore it to normal.

At the time of operation, the tail of the pancreas was grossly abnormal in its appearance. Since diabetes was not present, rather than resect this portion of the pancreas, it was implanted into the jejunum. In view of the extensive involvement of the pancreas, it is interesting that diabetes did not develop subsequently, although it has in another, similarly treated patient in whom the gross changes in the pancreas were not unlike those seen in this case. Since one cannot predict whether the remaining islet tissue in the tail of the pancreas is adequate to prevent diabetes, an attempt to prevent this complication is sufficiently important to justify the risk of recurrent pancreatitis that may be incurred by retaining the tail of the pancreas.

The graphic representation of the data obtained from the study of Patient S. D. (total pancreatectomy) is seen in Figure 4. The patient's daily diet consisted of 3521 Cal., 23.5 to 24.6 gm. of nitrogen and 124.5 to 133 gm. of fat. The mean daily urinary nitrogen output for the four periods was 13.3, 12.7, 15.7, and 15.7 gm., and the mean daily stool nitrogen for these periods was 12.2, 12.4, 6.3, and 7.6 gm., respectively. During Periods 1 and 2, when Viokase was withheld, the patient was in negative nitrogen balance, which became positive in Period 3, when the administration of Viokase was begun. In Period 4 the patient again went into negative nitrogen balance in spite of the continued use of

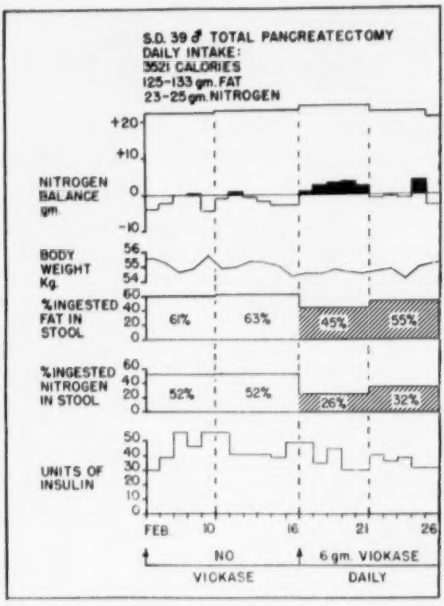


Fig. 4.—Metabolic chart.

Viokase. Although the administration of Viokase did not have a persistent effect upon the nitrogen balance in this patient, its effect upon the absorption of nitrogen was significant. During Periods 1 and 2 there was 52% and 52% of the ingested nitrogen in the feces, as compared with 26% and 32% during Periods 3 and 4, when Viokase was administered.

In this case Viokase had less effect upon the absorption of fat than it did upon the absorption of nitrogen. The mean daily fecal fat during the four periods was 81, 79, 60, and 71 gm., respectively. The fecal fat during each of these periods represented 61%, 63%, 45%, and 55% of the ingested fat. The negative nitrogen balance during Period 4, as contrasted with the positive balance in Period 3, can best be explained by the reduced nitrogen intake and the increased fecal nitrogen during the fourth period. During Period 4 the patient complained of abdominal cramps, which were thought to be related to his narcotic addiction. These may have had an influence upon nitrogen absorption.

Calcium and Phosphorus Balance Studies on Patient S. D. Following Total Pancreatectomy

Period	Mean Daily Calcium				Mean Daily Phosphorus			
	Diet, Gm.	Urine, Gm.	Stool, Gm.	Balance, Gm.	Diet, Gm.	Urine, Gm.	Stool, Gm.	Balance, Gm.
1	1.744	0.148	1.718	—0.122	2.491	1.655	1.109	—0.273
2	1.805	0.126	1.779	—0.100	2.525	1.651	1.124	—0.250
3	1.791	0.151	1.749	—0.109	2.769	1.647	1.063	+0.059
4	1.783	0.158	1.777	—0.152	2.554	1.632	1.043	—0.121

The calcium and phosphorus contents of the diet, urine, and stool were measured during each of the metabolic periods that Patient S. D. was studied. These data appear in the Table. There was no significant change in the urine, stool, or blood calcium throughout the study. It should be pointed out that fecal calcium was not reduced when fecal fat was decreased by Viokase. There was also no change in the urine phosphorus, but there was a reduction in fecal phosphorus during the last two periods, which accounted for an improvement in the phosphorus balance. It is of interest that the phosphorus balance was positive only in Period 3; this was also the only period when the patient was in positive nitrogen balance.

The graphic representation of the data obtained from the study of Patient E. M. (total pancreatectomy) is seen in Figure 5. The patient's daily diet consisted of 2226 Cal., 11.4 to 12.0 gm. of nitrogen and 110.4 to 123.8 gm. of fat. The mean daily urinary nitrogen output for the four periods was 5.0, 5.8, 4.1, and 3.8 gm., while the mean daily stool nitrogen for these periods was 3.4, 2.8, 5.8, and 5.3 gm., respectively. The nitrogen intake of this patient was approximately one-half that of the other two patients, and, in spite of the large fecal nitrogen losses, he maintained a positive nitrogen balance throughout the study. This was greater during Periods 1 and 2, when Viokase was administered. During the four periods that this patient was studied, there was 29%, 24%, 49%, and 45%, respectively, of the ingested nitrogen in the stools. The mean daily fecal fat during these periods was 43, 27, 69, and 57 gm., which represented 38%, 24%, 56%, and 46%, respectively, of the ingested fat. As was the case in the other two patients, administration of Viokase to this patient resulted in a beneficial effect upon the absorption of nitrogen and fat that was out of proportion to the improvement in nitrogen balance.

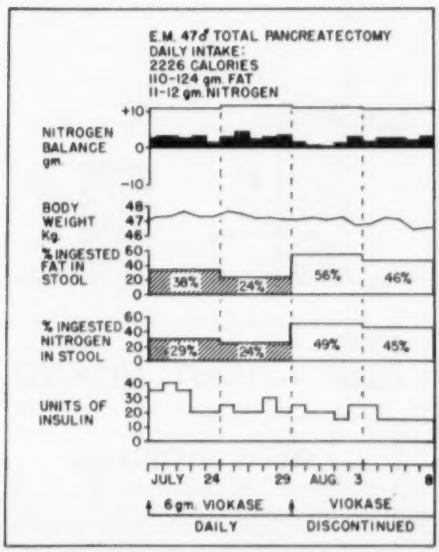


Fig. 5.—Metabolic chart.

Radioactive Absorption Studies.—Absorption of triolein and RISA without the concomitant administration of Viokase was studied in three patients, C. C., L. F., and V. H., who had undergone subtotal pancreaticoduodenectomy. Figure 6 shows the per cent of the administered dose of radioactivity in 1 ml. blood samples at three, six, and nine hours after the administration of triolein and at two, four, and six hours after the administration of RISA. Figure 6 also shows the per cent of the administered dose of radioactivity in 72-hour stool collections following the administration of triolein and

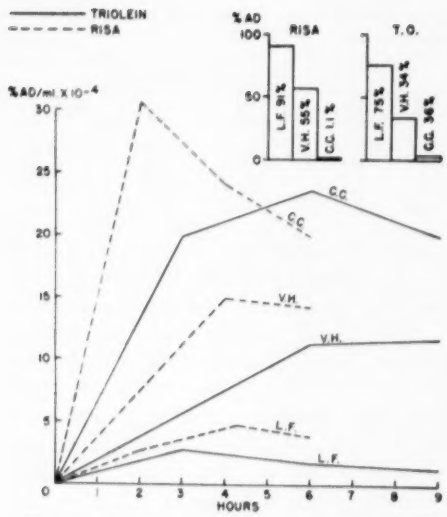


Fig. 6.—Comparison of the absorption of I^{131}-labeled triolein and RISA in three cases of subtotal pancreaticoduodenectomy as measured by the radioactivity of the blood and 72-hour stool collections.

RISA. The absorption of these materials, as indicated by the radioactivity appearing in the blood samples and stool collections, was within the normal range for Patient C. C. but was abnormal for Patients L. F. and V. H. The absorption of triolein and RISA by Patient V. H., however, lay intermediate between the very low values for Patient L. F. and the normal values for Patient C. C. With respect to the absorption deficit, it is of interest that at operation the remaining pancreas in Patient C. C. was grossly normal, while in Patients L. F. and V. H. this gland appeared grossly abnormal to a similar degree, although Patient L. F. subsequently became diabetic and Patient V. H. did not.

The effect of Viokase upon the absorption of triolein and RISA was evaluated in Patient V. H. Figure 7 shows the radioactivity appearing in the blood, and Figure 8 the radioactivity in the stools, following the administration of these substances with and without the administration of Viokase. The analyses of both blood and feces indicate that Viokase effectively increased the absorption of triolein and RISA. In our experience analyses of the stools are more indicative of the degree of absorption def-

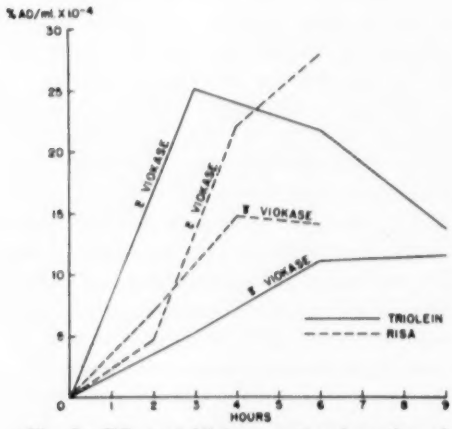


Fig. 7.—Effect of Viokase on the absorption of RISA and I^{131}-labeled triolein in Patient V. H. following subtotal pancreaticoduodenectomy as measured by the radioactivity of the blood.

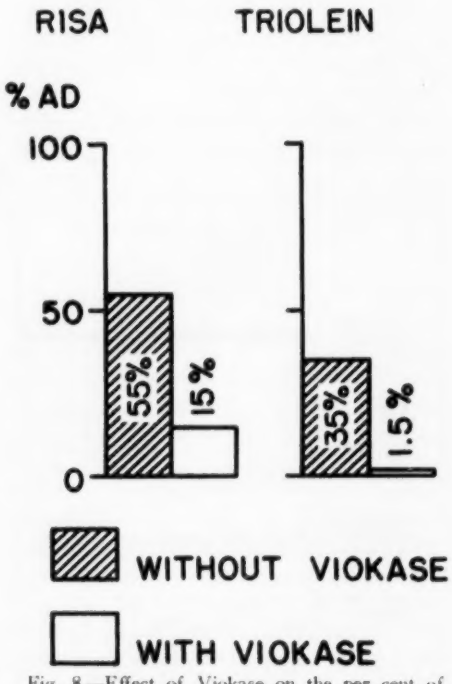


Fig. 8.—Effect of Viokase on the per cent of the administered dose of RISA and I^{131}-labeled triolein recovered in the 72-hour stool collections of Patient V. H. following subtotal pancreaticoduodenectomy.

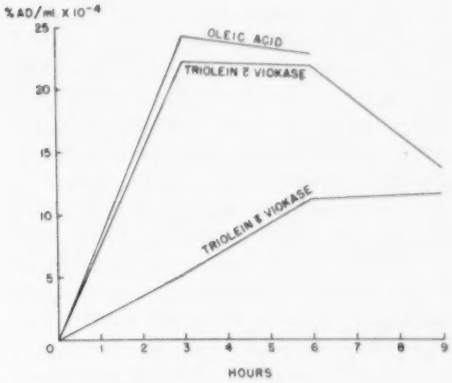


Fig. 9.—Comparison of the absorption of I^{131}-labeled oleic acid, triolein with Viokase, and triolein without Viokase in Patient V. H. following subtotal pancreaticoduodenectomy as measured by the radioactivity of the blood.

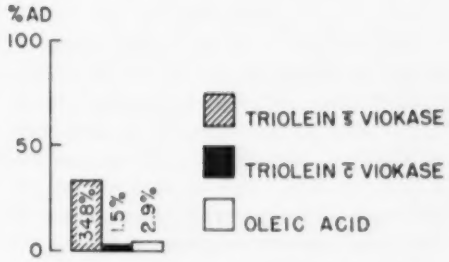


Fig. 10.—Comparison of the absorption of I^{131}-labeled oleic acid, triolein with Viokase, and triolein without Viokase as measured by the radioactivity of 72-hour stool collections.

icit present than are those of the blood. In this case the reductions of triolein in the stool from 34.8% to 1.5% and of RISA from 55.3% to 15.2% of the administered dose appear more indicative of the value of Viokase than is the comparison of the radioactivity in the respective blood samples.

The absorption of fat was further investigated by the use of radioactive oleic acid. The radioactivity in the blood and stools of Patient V. H. following the administration of triolein with and without the concomitant use of Viokase and of oleic acid without Viokase is seen in Figures 9 and 10, respectively. The absorption of triolein without Viokase was abnormally low, whereas, the absorptions of triolein with Viokase and oleic acid without Viokase were similar and in the normal range. The absorption of oleic acid also was studied in Patients E. M. and L. R. (total pancreatectomies). In these patients 9.3% and 8.2% of the administered doses of oleic acid appeared in the stools, as compared with 56.3% and 80.5% of the triolein administered without Viokase.

Iron Absorption.—The influence of pancreatectomy upon iron absorption was investigated in three patients with total pancreatectomy and one with subtotal pancreaticoduodenectomy using Fe^{59}. The results of these studies are seen in Figure 11. In the three cases of total pancreatectomy, 90%, 98%, and 92% of the administered dose of Fe^{59} was recovered in the stool, and 12%, 2%, and 2%, respectively, was incorporated into the red cells. The patient with subtotal pancreaticoduodenectomy had 84% of the dose of Fe^{59} recovered in the stools and 23% in the blood. The radioactivity in the blood normally expected with this method ranges from 5% to 10%. These results were interpreted as normal absorption of iron in the three cases of total pancreatectomy and as increased iron absorption in the patient with subtotal pancreaticoduodenectomy.

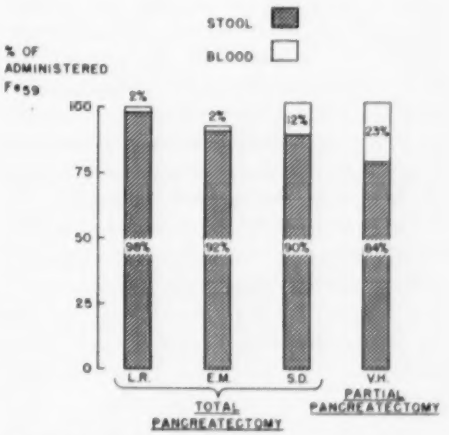


Fig. 11.—Per cent of administered Fe^{59} in feces and blood of three patients with total and one patient with subtotal pancreaticoduodenectomy.

Comment

There exists a difference of opinion as to the usefulness of pancreatin as replacement therapy for external pancreatic secretions. Most authors agree that such therapy is beneficial; some are of the opinion that it is of limited value because of the unpleasant gastrointestinal complaints encountered with the large amounts required to improve food absorption. Our data indicate that 6 gm. of pancreatin (Viokase) daily, taken in divided doses with meals, is well tolerated and improves nitrogen and fat absorption. Patients receiving Viokase are aware of this, because satiety is maintained on a lower caloric intake and the frequency and volume of the stools are reduced.

Although totally pancreatectomized patients can be maintained in good health and can lead useful lives, it is seldom, if ever, that their body weight will return to normal. The maintenance of these patients goes beyond the provision of insulin to control diabetes and pancreatic extracts to aid in digestion and absorption; indeed, the defects of pancreatic ablation may be protean. Failure of the body to utilize properly absorbed nitrogen may represent one of these defects.

External pancreatic replacement therapy significantly increased nitrogen and fat absorption in each of our patients studied either by the conventional method or by means of I^{131}-labeled fat or protein. In the three patients studied by the conventional metabolic method the effect of Viokase upon the nitrogen balance was less impressive than was its effect upon absorption. In each of these cases the increased absorption of nitrogen was offset by an increase in the urinary nitrogen. Assuming that these patients are chronically protein deficient, these data suggest that absorption of nitrogen in the pancreatectomized patient can more readily be made to approach normal than can the efficiency of its utilization.

Two of our patients, S. D. and L. R. (total pancreatectomy), were previously studied by Mellinkoff,[10] who showed that the administration of 250 cc. of 10% amino acids either orally or intravenously resulted in postabsorptive hyperaminoacidemia, which is suggestive evidence that amino acid "tolerance" is diminished in pancreatic diabetes. These patients also showed a hyperglycemic response to amino acids, as contrasted with the hypoglycemic response seen in nondiabetic patients. From these studies it was his conclusion that insulin is an important factor in the simultaneous utilization of amino acids and glucose. One can further postulate from these data that protein is ineffectually utilized by patients with pancreatic diabetes because of the body's inability to regulate the production of insulin to meet the increased requirements associated with the absorption of food.

The steatorrhea associated with pancreatic deficiency presents another of the difficult problems in the management of depancreatized patients. Several clinical studies[3,17] on pancreatectomized patients have shown that fatty acids constitute a larger proportion of fecal fat than triglycerides. This suggests that a defect in fat absorption may be equally as important as the defect in fat hydrolysis as the cause of steatorrhea in these patients. The careful studies of Annegers[1] on depancreatized dogs discredit these observations on patients, for he has shown that 66% of fecal lipid is triglyceride. Furthermore, he also pointed out that as a result of bacterial action fatty acids in the feces will increase as much as threefold when allowed to remain under refrigeration for five days. However, that some defect in absorption as well as a defect in hydrolysis is responsible for steatorrhea is suggested by Annegers' evidence[1] for an extradigestive function of pancreatic juice which is essential for complete assimilation of fat.

To study further the defect responsible for steatorrhea in depancreatized patients, radioactive oleic acid was employed. The absorption of oleic acid in these patients was superior to the absorption of triolein as indicated by both blood and stool analyses. Since the absorption of oleic acid as meas-

ured by the radioactivity in the blood was in the same range for normal patients as for those with pancreatic deficiency, a distinction between these two types of patients could only be made by a comparison of the radioactivity in the feces.

The ability of pancreatectomized patients to absorb oleic acid more efficiently than triolein was an unexpected finding, because it has previously been shown in normal dogs [1,11] and man [9] that absorption of triglyceride fat is greater than the absorption of fatty acids. In addition, it was demonstrated in depancreatized dogs by Annegers [1] and in pancreatic-duct-ligated dogs by Pessoa [11] that the defects in triglyceride and fatty acid absorption were of the same magnitude. Whether the discrepancy that exists in the absorption of fatty acids by our patients and the pancreatic-deficient dogs studied by others is the result of species differences or differences in technique is not known. Further investigation of substitutes for neutral fat in the diet of these patients is required.

The influence of the pancreas on the regulation of iron absorption has been of interest because of the role it may exert on the development of hemochromatosis. The results of several investigations, using mice and rats,[7] cats,[14] and dogs,[6] have shown that damage to the pancreas by either duct ligation or DL-ethionine increased iron deposition in the liver. These data were interpreted as representing an increased absorption of iron under conditions of inadequate pancreatic acinar function. It seemed worth while, therefore, to evaluate the possible effects pancreatic resection might have on the absorption of iron in man. These studies revealed that iron absorption was within normal limits for the patients with total pancreatectomy and elevated only in the patient with a subtotal pancreaticoduodenectomy without diabetes. These observations are too few from which to draw conclusions, but they suggest that caution must be taken in interpreting increased iron deposits in the liver of animals with inadequate pancreatic acinar function as evidence for increased iron absorption in depancreatized man.

The metabolic derangements created by total ablation of the pancreas, whether gradually by inflammation or suddenly by surgical removal, are profund and no doubt involve mechanisms that are not yet known. The problem of diabetes has not been dealt with in this paper, although it has been given considerable attention by others. The absence of a physiologically regulated supply of endogenous insulin undoubtedly is the most serious complication of the depancreatized patient. The increased sensitivity to insulin, which constitutes an ever-present threat of death, is the result of the body's inability to titrate its insulin supply to meet the fluctuating requirements throughout the day. It is also possible that failure to obtain maximum utilization of protein and fat, as well as carbohydrate, is related to the body's inability to regulate its insulin supply to meet these requirements.

In spite of the physiological defects that result from inadequate endocrine and exocrine functions of the pancreas, subtotal and total pancreaticoduodenectomies have been effective methods of treatment for a group of highly selected cases. The choice of total or subtotal pancreatectomy depends upon the degree of exocrine and endocrine deficiencies that exists as a result of inflammatory destruction of the gland's normal architecture. If the functional capacity of the pancreas has already become severely compromised, resection is a justifiable method of treatment, for perpetuation of the disease leads to a more crippling state for the patient than that which exists as a result of resection of the pancreas.

Summary

Subtotal and total pancreaticoduodenectomies are effective forms of treatment for chronic relapsing pancreatitis when there is marked dysfunction of the gland as a result of its architectural destruction.

Six patients with chronic relapsing pancreatitis treated by resection of the pan-

creas (three total and three subtotal) served as subjects for conventional and radioactive absorption studies.

Pancreatin (Viokase), 6 gm. a day, effectively reduced the fecal fat and nitrogen losses that resulted from inadequate external secretions of the pancreas.

The improvement in nitrogen balance which was associated with the administration of Viokase was not always commensurate with the degree of improvement in nitrogen absorption.

I^{131}-labeled triolein and radioiodinated (I^{131}) serum albumin (human) (RISA) were useful tools for the study of fat and protein absorption. Analysis of the radioactivity of the stools was a more reliable index of absorption than was the radioactivity of the blood.

Absorption of I^{131}-labeled oleic acid was significantly greater than the absorption of triolein. The importance of this observation as a therapeutic measure is unknown.

Iron-absorption studies using Fe^{59} were normal in three patients with total pancreatectomy and elevated in one patient with subtotal pancreaticoduodenectomy.

If the clinical indications of severe architectural destruction of the pancreas are adhered to as the indications for operation, the postoperative metabolic defects should not be significantly greater than the preoperative ones.

William G. Figueroa, M.D., performed the iron-absorption studies on these patients, and S. H. Bassett, M.D., provided the facilities of the research metabolic ward.

Veterans' Administration Center (25) (Dr. Jordan).

REFERENCES

1. Annegers, J. H.: Function of Pancreatic Juice and of Bile in Assimilation of Dietary Triglyceride, A. M. A. Arch. Int. Med. 93:9-22 (Jan.) 1954.

2. Cattell, R. B., and Warren, K. W.: Surgery of the Pancreas, Philadelphia, W. B. Saunders Company, 1953.

3. Dixon, C. F.; Comfort, M. W.; Lichtman, A. L., and Benson, R. E.: Total Pancreatectomy or Carcinoma of the Pancreas in a Diabetic Person, Arch. Surg. 52:619-639 (June) 1946.

4. Fallis, L. S., and Szilagyi, D. E.: Observations on Some Metabolic Changes After Total Pancreatoduodenectomy, Ann. Surg. 128:639-667 (Oct.) 1948.

5. Gaston, E. A.: Total Pancreatectomy, New England J. Med. 238:345-354 (March 11) 1948.

6. Kinney, T. D.; Finch, C. A.; Kaufman, N.; Hegsted, M., and Partington, P. F.: Relationship of the Pancreas to the Absorption of Iron, Am. J. Path. 26:746 (July) 1950.

7. Kinney, T. D.; Kaufman, N., and Klavins, J.: Effect of Ethionine-Induced Pancreatic Damage on Iron Absorption, J. Exper. Med. 102:151-156 (Aug.) 1955.

8. Longmire, W. P., Jr.; Jordan, P. H., Jr., and Briggs, J. D.: Experience with Resection of the Pancreas in the Treatment of Chronic Relapsing Pancreatitis, Ann. Surg. 144:681-695 (Oct.) 1956.

9. Malm, J. R.; Reemtsma, K., and Barker, H. G.: Comparative Fat and Fatty Acid Intestinal Absorption Test Utilizing Radioiodine Labeling: Results in Normal Subjects, Proc. Soc. Exper. Biol. & Med. 92:471-474 (July) 1956.

10. Mellinkoff, S. M.; Shibata, H. N.; Frankland, M., and Greipel, M.: Effect of Pancreatectomy upon Blood Sugar and Serum Amino Acid Concentration Following the Administration of Amino Acids, J. Lab. & Clin. Med. 48:529-532 (Oct.) 1956.

11. Pessoa, V. C.; Kim, K. S., and Ivy, A. C.: Fat Absorption in Absence of Bile and Pancreatic Juice, Am. J. Physiol. 174:209-218 (Aug.) 1953.

12. Priestley, J. T.; Comfort, M. W., and Radcliffe, J., Jr.: Total Pancreatectomy for Hyperinsulinism Due to an Islet-Cell Adenoma, Ann. Surg. 119:211-221 (Feb.) 1944.

13. Ricketts, H. T.; Brunschwig, A., and Knowlton, K.: Diabetes in a Totally Depancreatized Man, Proc. Soc. Exper. Biol. & Med. 58:254-255 (March) 1945.

14. Taylor, J.; Stiven, D., and Reid, E. W.: Experimental and Idiopathic Siderosis in Cats, J. Path. & Bact. 41:397-405 (Nov.) 1935.

15. Waugh, J. M.; Dixon, C. F.; Clagett, O. T.; Bollman, J. L.; Sprague, R. G., and Comfort, M. W.: Total Pancreatectomy: A Symposium Presenting 4 Successful Cases and a Report on Metabolic Observations, Proc. Staff Meet. Mayo Clin. 21:25-46 (Jan. 23) 1946.

16. Whipple, A. O.; Parsons, W. B., and Mullins, C. R.: Treatment of Carcinoma of Ampulla of Vater, Ann. Surg. 102:763-779 (Oct.) 1935.

17. Whitfield, A. G. W.; Gourevitch, A., and Thomas, G.: Metabolic Effects of Total Pancreatectomy in Man, Lancet 1:180-183 (Jan. 26) 1952.

Ductal and Vascular Factors in Etiology of Experimentally Induced Acute Pancreatitis

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This study was undertaken with the purpose of determining whether acute pancreatitis could be induced in dogs by ligation of the pancreatic ducts in face of an actively secreting gland and what bearing an associated disturbance in the blood supply of the pancreas had on the lesions so obtained. We were also interested in finding out whether a transitory disturbance of the blood supply of the pancreas produced by stimulation of the left splanchnic nerve would induce experimental pancreatitis, as had been reported by Mallet-Guy and others.[1-3] Very little evidence other than the recent experimental work of Lium and Maddock [4] has been offered to substantiate the hypothesis that acute pancreatitis may be due to obstruction of the outflow of pancreatic juice into the duodenum. The bulk of evidence from experimental studies is that ligation of the pancreatic ducts in experimental animals does not suffice to induce acute pancreatitis [5,6] and that an added factor, such as impairing the arterial blood supply of the gland [7] or supplying active trypsin [8] to the pancreas, is necessary in order to initiate the vicious circle. We suspect that previously reported failures to produce pancreatitis in the experimental animal can be accounted for by the state of inactivity of the gland at the time of the experiments, the external secretion being inhibited further by general anesthesia.

We found that ligation of the pancreatic ducts alone in recently fed dogs sufficed to produce gross and histologic lesions of acute pancreatitis. The latter occurred to a severer degree when ligation of the ducts was associated with disturbances in the blood supply of the pancreas, although these vascular disturbances by themselves did not appear to be sufficient to produce acute pancreatitis.

Read at the 64th Annual Meeting of the Western Surgical Association, Cincinnati, Nov. 30, 1956.

Fellow in Surgery, Mayo Foundation (Dr. Menguy); Section of Surgery (Dr. Hallenbeck); Section of Biochemistry (Dr. Bollman), and Section of Surgical Research (Dr. Grindlay), Mayo Clinic and Mayo Foundation. The Mayo Foundation, Rochester, Minn., is a part of the Graduate School of the University of Minnesota.

Methods

For this study 58 animals, 45 dogs and 13 cats, were used. We attempted to induce acute pancreatitis in these animals by obstructing the outflow of pancreatic juice into the duodenum by producing a disturbance of the blood supply of the gland or by a combination of these procedures.

Impairment of the outflow of pancreatic juice was produced by ligation of the pancreatic ducts.

Group 1.—This group consisted of seven dogs. The duodenal loop was mobilized through a midline abdominal incision, and both pancreatic ducts were divided between ligatures.

Impairment of pancreatic blood flow was achieved by ligating the major pancreatic veins or the major pancreatic arteries or by stimulation of the left splanchnic nerve.

Group 2.—In three dogs comprising this group the cephalic and caudal pancreaticoduodenal veins, as well as a small vein draining the tail of the pancreas into the portal vein, were divided between ligatures.

Group 3.—There were six dogs in this group. Through a midline abdominal incision the cephalic and caudal pancreaticoduodenal arteries supplying the head and the uncinate process of the gland were divided between ligatures. To render pancreatic ischemia complete, a small branch of the splenic artery supplying the tail of the gland was also ligated.

Group 4.—This group was composed of 13 cats and 7 dogs. In six cats and five dogs the experi-

ment was carried out with the animals under fasting conditions. In the remainder of the experiments the procedure was carried out after a meal. In the dogs the left splanchnic nerve was approached through the 10th thoracic interspace. The nerve was placed on a bipolar silver-wire electrode shielded with Lucite. The electrode was connected to a Grass stimulator. A 10-volt monophasic current with a frequency of 100 and a cycle duration of 5 msec. was used. Prior to closure of the stimulating current a small opening was made in the diaphragm, through which any changes in the color of the pancreas taking place during nerve stimulation could be observed. The stimulation was maintained for 15 minutes. In the cats the nerve was exposed in the abdomen at its point of emergence from under the fibers of the diaphragm. Stimulation was maintained for five minutes.

In the following groups a combination of duct obstruction and disturbance of pancreatic blood flow was produced.

Group 5.—In the seven dogs comprising Group 5, both pancreatic ducts were ligated, as in Group 1. In addition, the major pancreatic veins were ligated, as in Group 2.

Group 6.—This group consisted of seven dogs. Both pancreatic ducts were ligated, as in Group 1, after which we ligated the major pancreatic arteries, as in Group 3.

Group 7.—This group consisted of eight dogs. The splanchnic nerve was exposed through the 10th thoracic interspace. An electrode was placed around the nerve, and the chest was closed temporarily. The abdomen was then opened in the midline, and both pancreatic ducts were ligated, as in Group 1. The splanchnic nerve was stimulated for 15 minutes, after which the abdomen and the chest were closed.

In all the operative procedures, chloralose was used as anesthetic agent. It has been shown[9] that chloralose, in addition to not interfering with somatic reflexes, does not have a depressing action on autonomic, and particularly on vagal, centers. Pancreatic enzymatic secretion is in part dependent on vagal activity. In dogs we used 10 mg. of chloralose per kilogram of body weight, and in cats, 5 mg. per kilogram.

All the animals, unless otherwise specified, were fed one hour before the operation. The dogs were given from 400 to 500 gm. of horse meat, and the cats were fed cream and meat ad libitum. The procedures were performed under strict aseptic conditions, and penicillin was left in the peritoneal cavity and administered daily thereafter. Samples of blood were withdrawn for plasma amylase determinations before induction of anesthesia and at 12, 24, 48, and 72 hours postoperatively. During the postoperative period the general behavior of the animals, their appetite for food, and so forth, were observed. Most of the animals were killed at 48 or 72 hours after operation. A few were killed at 24 hours in order to enable us to evaluate early pathologic changes. At necropsy the quality and the quantity of peritoneal exudate were recorded, as well as the degree of extrapancreatic fat necrosis, if any. The pancreas was removed *in toto* and placed in 10% solution of formalin. After adequate fixation, sections were taken from standard areas of the gland and were stained with hematoxylin and eosin.

Determinations of plasma amylase were made by incubating diluted plasma with soluble starch for 15 minutes at 37 C. The maltose thus liberated was measured by the ferricyanide method of Nørby as modified by Lagerlöf.[10] Each milligram of maltose liberated from the starch substrate represented 1 unit of plasma amylase. The average value for the plasma amylase before induction of anesthesia for the various procedures was 16.7 units, with a standard deviation of 5.7 units.

The following criteria were used for the evaluation of our experimental results: (1) gross evidence of fat necrosis in and around the pancreas and gross evidence of pancreatic hemorrhage; (2) microscopic alterations consisting in interstitial edema, inflammatory exudate, interstitial hemorrhage, fat necrosis, and pancreatic parenchymal necrosis, and (3) elevation of plasma amylase.

Results

A. Obstruction to Outflow of Pancreatic Juice.—1. Ligation of Pancreatic Ducts: All the animals in this group were killed 72 hours after the operation. The dogs were quite ill after the procedure, but it was felt that they would not have died had they not been killed electively. At necropsy varying amounts of serosanguineous fluid were found in the peritoneal cavity in all the animals. Except in one animal there were innumerable flecks of fat necrosis in the pancreas and the surrounding tissues—transverse mesocolon and duodenal and jejunal mesentery. The omentum had a "caked" appearance. In one of the animals the lesions of fat necrosis involved the entire peritoneal cavity. The capsule of the pancreas was invariably elevated by edema fluid also infiltrating between and separating the pancreatic lobules. In two animals this subcapsular fluid was grossly bloody. In the other animals there were scattered

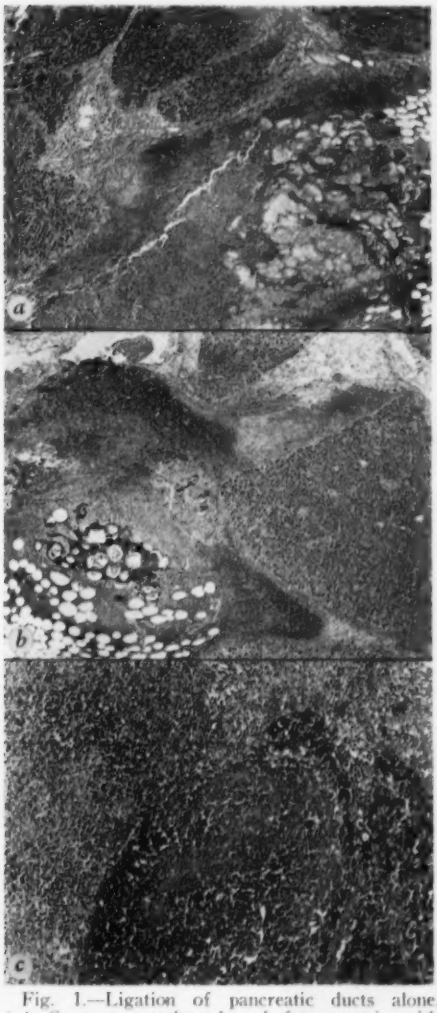
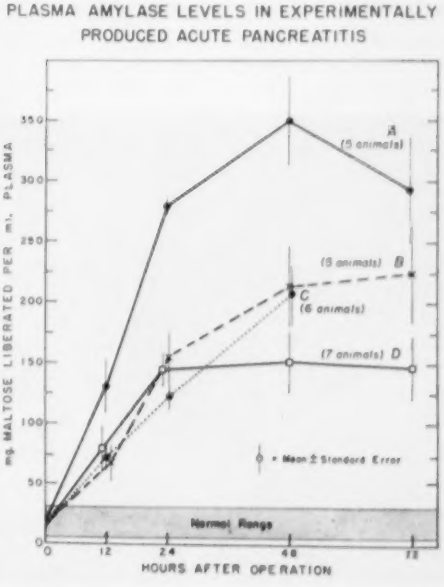


Fig. 1.—Ligation of pancreatic ducts alone. (*a*) Severe parenchymal and fat necrosis with exudative reaction. Note the destruction of the peripheral groups of acini of neighboring lobules on the right upper side of the section. Hematoxylin and eosin; reduced to 69% of mag. ×30. (*b*) Same as (*a*) plus hemorrhage. Hematoxylin and eosin; reduced to 69% of mag. ×30. (*c*) Parenchymal necrosis with replacement of acinar cells by amorphous material and inflammatory cells. Hematoxylin and eosin; reduced to 69% of mag. ×150.

areas of petechial hemorrhage over the surface of the gland, and evidence of hemorrhage in the intralobular septa was apparent on gross sections of the pancreas.

Except in one animal, in which sections showed alterations typical of interstitial pancreatitis, all the microscopic features of acute pancreatitis were present. Pancreatic parenchymal necrosis was a definite feature (Fig. 1*a*, *b*, and *c*). Entire pancreatic lobules or portions thereof were destroyed and replaced by sheets of inflammatory cells. Autodigestion of pancreatic tissue seemed to proceed from the periphery of the pancreatic lobules, where the groups of acini bordering the intralobular septa were the most involved, toward the center of the lobules, where only cellular alterations, such as hydropic degeneration of the cytoplasm, were seen. There were also scattered foci of necrosis situated deep in the lobules where groups of acini had been destroyed and replaced by a pink-staining amorphous substance (Fig. 1*c*). There were marked interlobular and intralobular edema and inflammatory exudate. Fat necrosis, already apparent grossly, was a constant finding. Microscopic hemorrhage was present to a marked degree in four of seven specimens. The ducts were invariably dilated.

Fig. 2.—Mean plasma amylase curves after (*A*) ligation of both pancreatic ducts alone, (*B*) ligation of ducts and of veins, (*C*) ligation of ducts and stimulation of left splanchnic nerve, and (*D*) ligation of ducts and of arteries.



In five animals in which plasma amylase was determined postoperatively, a pronounced elevation in enzyme levels was present (Fig. 2).

B. Impairment of Pancreatic Blood Supply.—In general, these animals appeared to be in relatively good health after the operation and were hungry for food the following day.

1. Ligation of Major Pancreatic Veins: The three animals in this group were killed at 24, 48, and 72 hours, respectively. The last two had no change in the postoperative plasma amylase levels, whereas in the first animal the plasma amylase was normal at 12 hours and had reached 74 units at 24 hours. In none of the animals was any peritoneal exudate or any gross fat necrosis in or around the pancreas observed at necropsy. Two of the animals had small hemorrhagic infarcts localized to the tail of the pancreas. Otherwise the pancreas appeared congested. The only microscopic finding of note was moderate interstitial edema present in all three specimens. In two animals there was some hemorrhagic necrosis around the small infarcts in the tail of the pancreas. Scattered areas of focal necrosis were seen in one animal (Fig. 3). There was no spreading pancreatitis. The ducts were normal.

2. Ligation of Major Pancreatic Arteries: Of the six animals, one died of aspiration pneumonitis 24 hours after the procedure. The others appeared in good health. Two were killed at 24 hours and three at 72 hours. The plasma amylase levels were normal in all except one, in which a slight elevation was found in the 72-hour sample of blood. In none of the animals was there any gross evidence of pancreatitis at necropsy. Microscopically, scattered foci of ischemic necrosis were present in four of six specimens (Fig. 4). These foci were surrounded by moderate edema and inflammatory exudate in two specimens. Otherwise the adjacent pancreatic lobules appeared normal. There was no spreading pancreatitis (Fig. 4).

3. Stimulation of Left Splanchnic Nerve: This group consisted of 20 animals, 13 cats and 7 dogs. When the stimulating current was closed, an immediate blanching of the pancreas was apparent. This lasted for one to two minutes, after which the pancreas regained its normal color, even though the stimulation was being continued. After the operation all the animals appeared in good health except for three cats which died of an overdose of chloralose. The postoperative plasma amylase levels measured in the seven dogs remained normal.

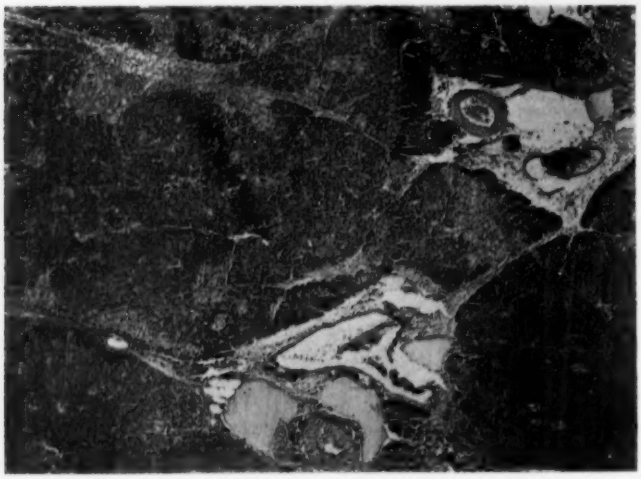


Fig. 3.—Ligation of major pancreatic veins alone. Multiple foci of parenchymal necrosis. Minimal inflammatory exudate. No spreading pancreatitis. Hematoxylin and eosin; ×30.

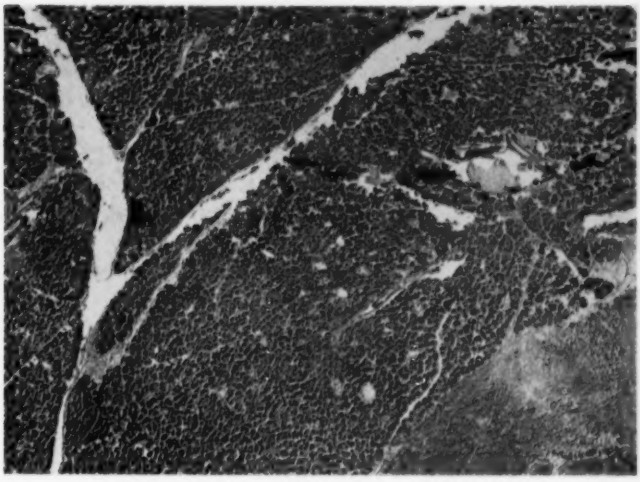


Fig. 4.—Ligation of major pancreatic arteries alone. Area of ischemic necrosis at lower right-hand corner of the section. By contrast, the remainder of the section shows no spreading pancreatitis. Hematoxylin and eosin; × 30.

The animals were killed from 24 to 72 hours after the operation. Invariably we were impressed at necropsy by the dusky, cyanotic appearance of the pancreas. This was the only abnormal gross finding. By contrast, the microscopic alterations were minimal. Marked vascular congestion and, in three animals, some edema and interstitial hemorrhage were the only findings of note (Fig. 5). Feeding the animals prior to the experiment did not appear to have any bearing on the results.

C. Obstruction of Outflow of Pancreatic Juice Associated with Disturbances in Blood Supply of the Pancreas.—1. Ligation of Pancreatic Ducts and of Major Pancreatic Veins: This group consisted of seven dogs. The animals were extremely ill after the operation. Four were moribund at the time that they were killed. One animal was killed at 24 hours, three at 48 hours, and three at 72 hours. Postoperative plasma amylase levels were obtained in five animals. In all there was a pronounced elevation, although the mean curve was lower than that measured in the animals that had undergone ligation of the pancreatic ducts alone (Fig. 2). In all the animals large amounts of

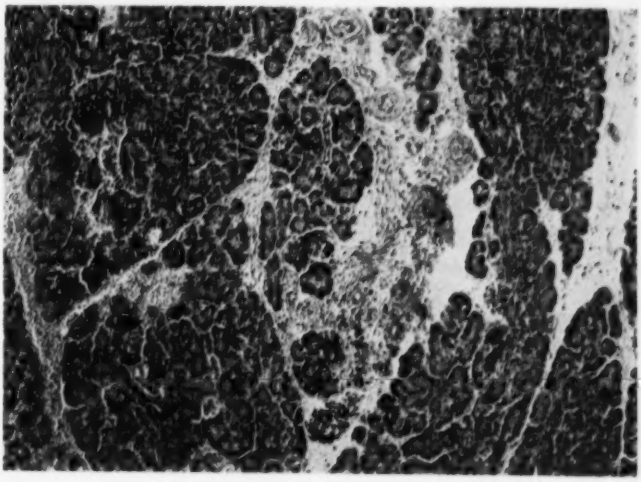


Fig. 5.—Stimulation of left splanchnic nerve alone. Moderate interlobular and intralobular edema and hemorrhage. This is not acute pancreatitis. Hematoxylin and eosin; × 100.

bloody fluid were present in the peritoneal cavity. Innumerable flecks of fat necrosis were seen in the pancreas and surrounding structures in all the animals. In three, the lesions of fat necrosis extended to the entire peritoneal cavity. All the specimens were grossly hemorrhagic. In three animals hemorrhagic necrosis had destroyed the entire body and tail of the pancreas. In four animals a pseudocyst was found. This consisted of adhesions of loops of small bowel, omentum, and transverse mesocolon to the tail of the pancreas. When these adhesions were broken down, a small pocket containing bloody fluid under tension was revealed. The walls of these "cysts" were caked by fat necrosis.

Microscopically, all the features of acute pancreatitis were present, and to a more marked degree than in Group 1. Necrosis of pancreatic tissue was especially pronounced and in certain areas took on the appearance of autodigestion, whereas in others the mechanical action of hemorrhage (similar to the action of a jet of water playing on sand) seemed to be responsible for the architectural alterations (Fig. 6). The ducts were dilated in all of the specimens.

2. Ligation of Pancreatic Ducts and of Major Pancreatic Arteries: Seven dogs were in this group. One animal died of acute pancreatitis 24 hours after the operation. The others survived 72 hours, but four were moribund at the time that they were killed. Plasma amylase levels obtained in the seven animals were elevated (Fig. 2). The mean curve was lower than that measured in Group 1. Marked peritoneal hemorrhage was present in six animals, although to a slighter degree than in Group 5. In all the animals there were innumerable flecks of fat necrosis in and around the pancreas. In five animals the lesions of fat necrosis were widespread throughout the entire peritoneal cavity. Again the microscopic features of acute pancreatitis were present in all the specimens and to a greater degree than was observed in Groups 1 and 5. Only interstitial and intralobular hemorrhages were less pronounced than in Group 5. On the other hand, pancreatic parenchymal necrosis was extremely severe (Fig. 7). The ducts were dilated in all the specimens.

3. Ligation of Pancreatic Ducts and Stimulation of Left Splanchnic Nerve: There were eight dogs in this group. None died of acute pancreatitis. Plasma amylase levels measured in six animals showed a definite elevation (Fig. 2). One animal was killed at 72 hours; the remainder, at 48 hours. Gross and microscopic features of actue pancreatitis were present in all the animals. The degree of pathologic altera-

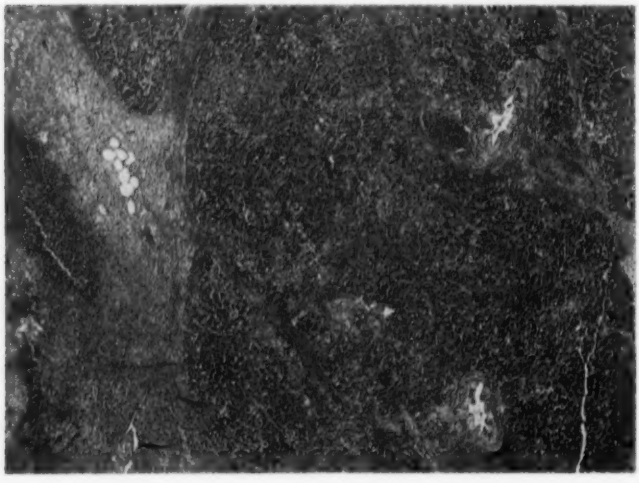


Fig. 6.—Ligation of pancreatic ducts and of major pancreatic veins. Severe parenchymal necrosis on the left-hand side of the section adjacent to an area of hemorrhagic necrosis. Hematoxylin and eosin; ×30.

Fig. 7.—Ligation of pancreatic ducts and of major pancreatic arteries. Severe parenchymal necrosis. The pancreatic acinar tissue is completely destroyed and is replaced by sheets of inflammatory cells. The pronounced hemorrhage is not apparent under this low power. Hematoxylin and eosin; ×30.

tions was intermediate between those observed in Group 1 and those observed in Groups 5 and 6.

Comment

We feel that the crux of our study was the finding that obstruction of the outflow of pancreatic juice in the face of an actively secreting gland was sufficient to produce all the gross and microscopic features of acute pancreatitis, including pancreatic parenchymal necrosis. We suspect that previously reported failures to induce acute pancreatitis in laboratory animals by this method can be attributed to the fact that the gland was in a state of inactivity at the time of the experiments, with the anesthetic factor intervening further to depress external pancreatic secretion. Although in some instances [5,11] an attempt was made to stimulate pancreatic secretion, the use of secretin defeated the purpose, for pancreatic juice secreted in response to secretin is very low in enzyme content. The specific lesions of acute pancreatitis, that is, pancreatic parenchymal necrosis, fat necrosis, and vascular necrosis with hemorrhage, could not, a priori, be expected to occur under such conditions. The only *raison d'être* of this type of research is to refer experimental findings to clinical conditions. Since human beings, in whom acute pancreatitis occurs spontaneously, eat at least three meals a day and since acute pancreatitis often occurs after a heavy meal, it is only logical to test the factor presumed to cause pancreatitis on laboratory animals that are in conditions at least similar to those under which pancreatitis occurs spontaneously in the human, that is, an actively secreting pancreas.

It can be objected that necropsy studies of patients who have died of acute pancreatitis have only infrequently revealed an obvious cause of obstruction of the pancreatic ducts, such as a stone at the common papilla. One must then invoke a spasm of the sphincter of Oddi. This concept is far from being hypothetical. It has been shown that biliary pressures reflecting complete sphincteric obstruction can occur in human subjects after the administration of opiates.[12,13] In studies carried out in dogs [14] we have shown that the pancreatic intraductal pressure can rise to levels approximating the maximal secretory pressure of the pancreas following the administration of morphine or the injection of alcohol into the duodenum. Owing to the absence of a pressure-regulating mechanism, such as the biliary tree has in the gallbladder, the pancreatic intraductal pressure is very susceptible to sudden variations in the tone of the pancreatic sphincter mechanism.

Ligation of the pancreatic ducts alone did not in our experience produce that fulminating, gangrenous form of acute hemorrhagic pancreatitis that is not infrequently observed in the human. We suspect that the reason for this lies not so much in the existence of a different cause or an added factor as in the different anatomic dispositions assumed by the pancreas in the human being and in the dog. In the latter, the pancreas lies in the mesentery of the duodenum, and pancreatic juice is free to escape from all sides into the peritoneal cavity, the duodenum not being bound down by the parietal peritoneum. In our experiments a marked "weeping" of fluid through the capsule of the pancreas was always visible shortly after ligation of the ducts. Thus, accumulation of pancreatic juice in the vicinity of the pancreas with concentration and autoactivation of pancreatic enzymes is, to a certain extent, prevented. Such a mode of escape does not exist in the human, in whom the pancreas is largely a retroperitoneal organ. Accumulation of pancreatic juice around the pancreas could conceivably lead to a high local tissue pressure, which by itself could be a cause of vascular, particularly of venous, stasis. Also, accumulation and concentration of pancreatic juice could lead to blood vessel thrombosis and necrosis.

When these factors, ischemia and venous stasis, were produced artificially in conjunction with duct obstruction, the degree of pancreatitis that occurred was very severe. However, we repeat that this added factor was not a *sine qua non*, and that ductal obstruction alone was sufficient to produce typical acute pancreatitis.

The lower plasma amylase levels in the groups of animals that had a severer degree of pancreatitis (ligation of the pancreatic ducts in conjunction with ligation of the major pancreatic veins or arteries) were probably due to the greater destruction of pancreatic secretory tissue. This correlates with the clinical impression that the serum amylase level is not always proportional to the severity of pathologic alterations.

Local pancreatic vascular disturbances alone, either ischemia or venous stasis, produced focal necrosis, fat necrosis, and hemorrhage. In no instance was the characteristic gross and microscopic picture of diffuse spreading pancreatitis seen. The delayed and moderate elevation of plasma amylase that was measured in two animals in which only vascular disturbances had been produced showed that even in the absence of spreading pancreatitis and of duct obstruction localized necrosis of pancreatic tissue can lead to a rise of plasma amylase.

In our hands stimulation of the left splanchnic nerve did not produce acute pancreatitis either in the cat or in the dog. This was at variance with what had been reported by Mallet-Guy and others.[1-3] Comparison of microscopic alterations observed in a few of our animals after nerve stimulation, with photomicrographs published by Mallet-Guy and his associates, showed that our findings were essentially similar to theirs. The whole difference was one of definition.

Summary

Experiments were carried out on cats and dogs in order to evaluate such factors as ductal obstruction and local vascular disturbances in the pathogenesis of acute pancreatitis.

When both pancreatic ducts were ligated in recently fed dogs, lesions of acute pancreatitis, including pancreatic parenchymal necrosis, as well as an elevation of plasma amylase, occurred. When ligation of the ducts was combined with ligation of the major pancreatic arteries or veins or with stimulation of the left splanchnic nerve, acute pancreatitis of a severer degree ensued; by contrast, the concomitant elevation of plasma amylase was less pronounced. Vascular disturbances alone, brought about by ligation of the pancreatic arteries or veins or by stimulation of the left splanchnic nerve, did not suffice to induce acute pancreatitis.

Mayo Clinic and Mayo Foundation.

REFERENCES

1. Mallet-Guy, P.; Feroldi, J., and Reboul, E.: Recherches expérimentales sur la pathogénie des pancréatites aiguës: Leur provocation par l'excitation du nerf splanchnique gauche, Lyon chir. 44: 281-301 (May-June) 1949.

2. Mallet-Guy, P.: Sphincterotomy and Splanchnicectomy in the Treatment of Chronic Relapsing Pancreatitis, A. M. A. Arch. Surg. 72:366-370 (Feb.) 1956.

3. Longo, O. F.; Sosa Gallardo, C. A., and Ferraris, A.: Contribution à la pathogénie des pancréatites aiguës, Lyon chir. 45:297-305 (April) 1950.

4. Lium, R., and Maddock, S.: Etiology of Acute Pancreatitis: An Experimental Study, Surgery 24:593-604 (Oct.) 1948.

5. Popper, H. L., and Necheles, H.: Edema of the Pancreas, Surg. Gynec. & Obst. 74:123-124 (Jan.) 1942.

6. Gibbs, G. E., and Ivy, A. C.: Early Histological Changes Following Obstruction of Pancreatic Ducts in Dogs: Correlation with Serum Amylase, Proc. Soc. Exper. Biol. & Med. 77:251-254 (June) 1951.

7. Popper, H. L.; Necheles, H., and Russell, K. C.: Transition of Pancreatic Edema into Pancreatic Necrosis, Surg. Gynec. & Obst. 87:79-82 (July) 1948.

8. Powers, S. R., Jr.; Brown, H. H., and Stein, A.: Pathogenesis of Acute and Chronic Pancreatitis, Ann. Surg. 142:690-695 (Oct.) 1955.

9. La Barre, J., and Wauters, M.: Contribution à l'étude de l'influence des hypnotiques sur le tube digestif: Action du chloralose et du barbital sur la sécrétion gastrique, Arch. internat. pharmacodyn. 44:178-188 (Jan. 20) 1933.

10. Lagerlöf, H. O.: Pancreatic Function and Pancreatic Disease Studied by Means of Secretion, Acta med. scandinav., Supp. 128, 1942.

11. Radakovich, M.; Pearse, H. E., and Strain, W.: Study of the Etiology of Acute Pancreatitis (Abstr.), S. Forum 2:588, 1952.

12. McGowan, J. M.; Butsch, W. L., and Walters, W.: Pressure in the Common Bile Duct of Man: Its Relation to Pain Following Cholecystectomy, J. A. M. A. 106:2227-2230 (June 27) 1936.

13. Curreri, A. R., and Gale, J. W.: Effect of Analgesics and Antispasmodics on Common Duct Pressures, Ann. Surg. 132:348-361 (Sept.) 1950.

14. Menguy, R. B.; Hallenbeck, G. A.; Bollman, J. L., and Grindlay, J. H.: Pancreatic and Biliary Intraductal Pressures, S. Forum 6:359-363, 1956.

Effect of Pancreatic Secretions on the Gallbladder

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Experimental investigation of the effect of the presence of pancreatic ferments in the biliary system was first reported in 1917 by Blad,[1] who injected duodenal juices into the gallbladders of dogs during his study of the pathogenesis of nonperforative bile peritonitis. Since then several investigators have injected pancreatic juice into the gallbladder and bile duct system, with varying results.[2-5] Bisgard and Baker[6] ligated the common bile duct of young goats near the duodenum, resulting in a mixing of bile and pancreatic enzymes in both the gallbladder and the pancreas and producing cholecystitis and pancreatitis. They observed that pancreatic ferments alone did not produce inflammation of the biliary tract, but when pancreatic enzymes were in the gallbladder, together with a condition of stasis, cholecystitis invariably developed. More recently Reid[7] anastomosed an isolated segment of duodenum containing the main pancreatic duct to the gallbladder in dogs with and without ligating the cystic duct and found that pancreatic ferments combined with bile stasis would experimentally produce cholecystitis. It is apparent that experimental investigations in the past have been directed primarily toward a study of acute gallbladder disease produced by pancreatic ferments in the presence of bile stasis.

The following experimental study was designed to observe the effects of prolonged exposure of the gallbladder to pancreatic secretions.

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From the Surgical Research Laboratories of the University of California School of Medicine.

Read at the 64th Annual Meeting of the Western Surgical Association, Cincinnati, Nov. 30, 1956.

Experiments on Goats

Fifteen young goats, 3 to 4 months of age, were selected for the first part of this study because of the anatomical arrangement of their ductal system, in which the pancreatic duct enters the common bile duct some distance from the duodenum. All animals were anesthetized with intravenous pentobarbital sodium solution, and a low tracheotomy was performed to prevent anoxia resulting from accumulated upper tracheal secretions during the surgical procedures.* Aseptic surgical technique was used for all experimental operations. In two of the animals only a cholecystectomy was done in order to compare the normal histology of the goat's gallbladder with that of the experimental animals. In the other 13 goats a Roux-Y cholecystojejunostomy was performed, and intestinal continuity was reestablished with an end-to-side jejunojejunostomy. In each of three animals only a Roux-Y cholecystojejunostomy was performed as a control, to test the effect on the gallbladder of a cholecystojejunostomy without diverting the pancreatic ferments through the bile ducts and gallbladder. In each of the other 10 goats the same type of cholecystojejunostomy was performed, and, in addition, the common duct was divided distal to its juncture with the pancreatic duct and ligated near its site of entrance into the duodenum, thus allowing pancreatic juice to pass into and through the gallbladder (Fig. 1).

At the completion of each experiment the animals were examined to determine the patency of the cholecystojejunostomy, and representative tissues were obtained from the gallbladder,* liver, pancreas, and common bile duct for histological study.

The two normal gallbladders were blue with very thin, translucent walls. In each case the gallbladder mucosa was red with delicate trabeculations. Microscopic examination (Fig. 2) revealed that the gallbladder

* All the gallbladder specimens, in both the goats and the dogs, were removed while the animals were anesthetized but still living. The gallbladders were immediately incised longitudinally; the bile was removed from them, and within one minute after excision they were placed in neutral formalin solution in order to avoid tissue autolysis.

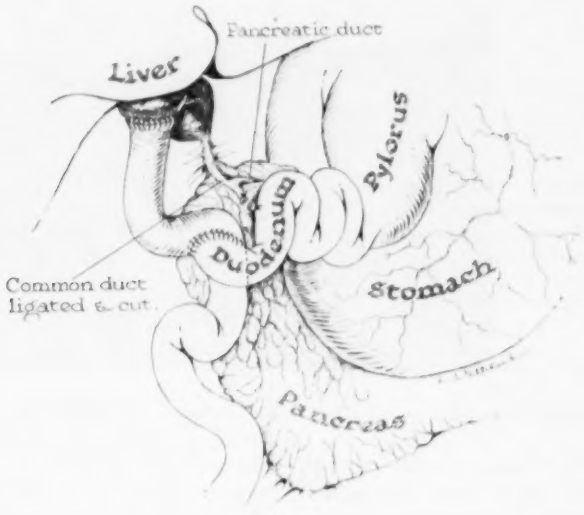


Fig. 1.—Diagram of the completed operative procedure that results in the passage of pancreatic secretions through the gallbladder of the goat.

mucosa consisted of tall columnar epithelial cells with a moderate number of villous projections and folding of the mucosa to form mucosal crypts; the submucosa contained a few round cells and an occasional group of small glands; the muscularis was attenuated and very thin; there appeared to be no definite serosa.

The three control animals (Roux-Y cholecystojejunostomy without ligation of common duct) were killed 12 weeks postoperatively. Pancreatic ferments were not found in the gallbladders of these three control animals. The gallbladders appeared blue and semitranslucent with slightly thickened walls, and the mucosa was red with coarse trabeculations. On microscopic examination the mucosa of the gallbladder was found to consist of tall columnar epithelial cells with glandular proliferation that appeared to be a metaplasia to simulate intestinal mucosa; the submucosa was slightly thickened, but there was no increase in round cells; the muscularis was moderately hypertrophied; the serosa was unchanged. The pathologic interpretation was normal gallbladder with

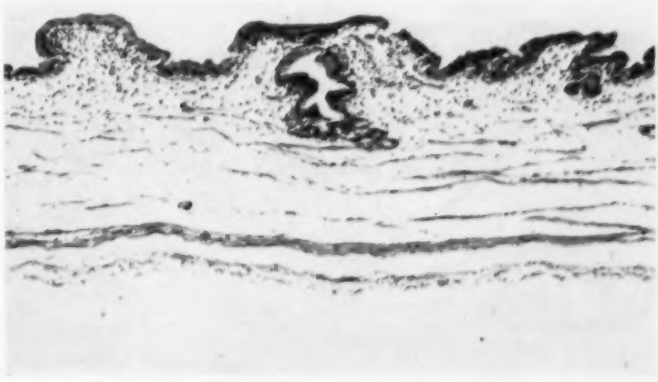


Fig. 2. — Photomicrograph of a section of normal gallbladder of the goat.

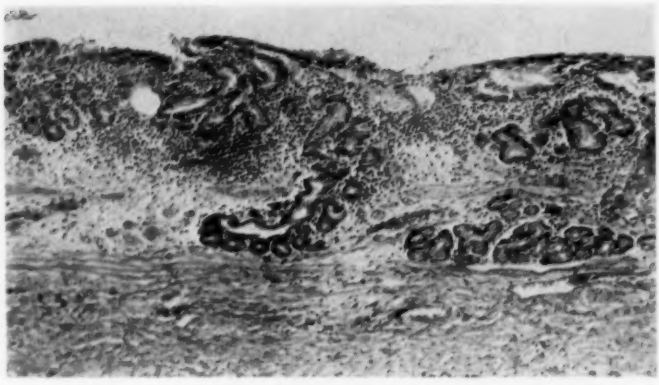


Fig. 3. — Photomicrograph of a section of gallbladder from Goat 4, with pancreatic juice passing through the gallbladder for six weeks postoperatively, showing moderately severe chronic cholecystitis.

mucosal metaplasia to simulate intestinal mucosa.

Five of the experimental animals (Roux-Y cholecystojejunostomy with ligation of the common bile duct) were killed 6 weeks and five were killed 12 weeks after operation. In all these animals pancreatic ferments were found in the gallbladders, and all the cholecystojejunostomy anastomoses were patent with adequate stomas. No gallstones were found. Gross and microscopic examination of the livers, common bile ducts, pancreases, and Roux-Y segments of jejunum revealed no evidence of inflammation or other pathologic change.

In the five goats that were killed six weeks postoperatively, the gallbladders were bluish gray and slightly contracted with moderately thickened, semitranslucent walls, and the mucosa appeared red with flattened trabeculations. Microscopic examination of these gallbladders revealed desquamation and flattening of the epithelium of the mucosa with moderate glandular hyperplasia, and a marked increase in lymphocyte and plasma-cell infiltration of the submucosa; the submucosal glands were increased, and there was penetration of these glands into the superficial muscularis; there were moderate hypertrophy and infiltration of the muscularis with lymphocytes and plasma cells; the subserosal area showed increased fibrosis. The pathologic interpretation was chronic cholecystitis, moderate degree (Fig. 3).

The gallbladders of the five goats that were killed 12 weeks postoperatively were gray and contracted, with thick, rigid, opaque walls. The mucosa of these gallbladders was brownish in color and without trabeculation. Microscopic examination showed desquamation and flattening of the

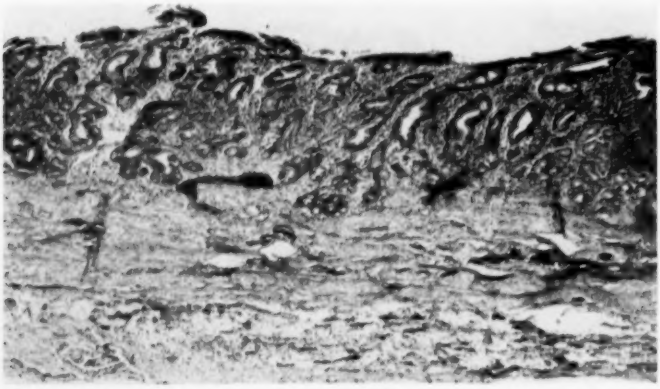


Fig. 4. — Photomicrograph of a section of gallbladder from goat 9, with pancreatic juice passing through the gallbladder for 12 weeks postoperatively, showing very severe chronic cholecystitis.

epithelium of the gallbladder mucosa with marked glandular hyperplasia; the submucosa was densely infiltrated with lymphocytes, plasma cells, and fibrous tissue. There were marked proliferation and penetration of the submucosal glands into the gallbladder muscularis, which was considerably thickened, hyperplastic, and fibrotic. There was marked fibrosis of the gallbladder serosa and subserosa. The pathologic interpretation was chronic cholecystitis, marked degree (Fig. 4).

Experiments on Dogs

A second series of experiments was done on dogs because they rarely develop cholecystic disease spontaneously, whereas goats occasionally do so after they reach the age of 9 months.[6] In this series of experiments, 6 dogs in which no surgical procedures were done served as controls, and 14 adult mongrel dogs were used for testing the effect of pancreatic juice on the gallbladder. General anesthesia was obtained with intravenous pentobarbital sodium solution, and aseptic precautions were followed throughout the surgical procedures. The ventral rudiment of the pancreas was identified in the mesentery of the duodenum. The pancreas was then dissected free from the duodenum, with careful ligation of the pancreaticoduodenal vessels, thus exposing the lesser pancreatic duct where it joined the common bile duct and the major pancreatic duct a few centimeters distal to the juncture of the lesser pancreatic and common bile ducts. The lesser pancreatic duct was divided, and both ends were ligated. The major pancreatic duct was divided but only its distal end ligated (Fig. 5*A*). The open proximal end of the major

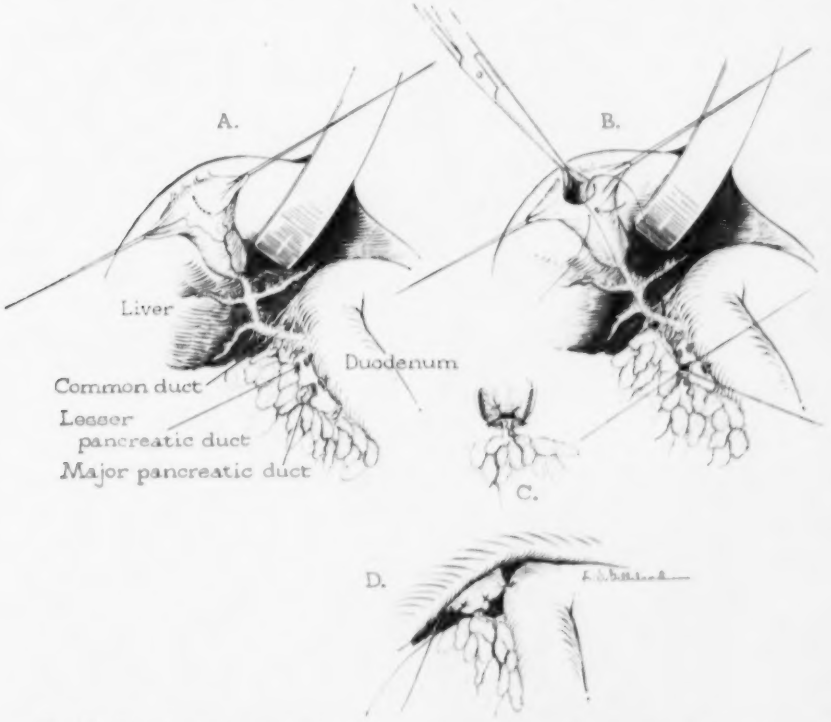


Fig. 5.—Diagrams of the operative procedure used to divert pancreatic secretions through the gallbladder of the dog. *A*, the major and lesser pancreatic ducts have been dissected out and divided. Both ends of the lesser pancreatic duct and the distal end of the major pancreatic duct have been ligated. *B*, four sutures have been placed in the major pancreatic duct, and both ends of each suture are introduced through the cholecystostomy wound and brought out from the mucosa to the serosa at four equidistant points around the cholecystostomy incision. *C*, sagittal section through the gallbladder showing the position of the pancreatic duct within the gallbladder. *D*, completed procedure. A single interrupted suture has been placed between the gallbladder and the duodenum to prevent tension on the pancreaticocholecystostomy anastomosis.

pancreatic duct was implanted into the fundus of the gallbladder (Fig. 5*B*, *C*, and *D*). Seven of the dogs were killed after three months and the other seven after six months of continuous exposure of the gallbladder to pancreatic ferments. At autopsy the patency of the major pancreatic ducts was determined by direct examination (Fig. 6) and by finding pancreatic enzymes in the gallbladder bile. No gallstones were found. Representative microscopic sections were prepared from the fundus and cystic duct regions of the gallbladders,† the pancreases, the livers, and the common bile ducts for histological study. Gross and microscopic examination of the livers and common bile ducts of the dogs was within normal limits.

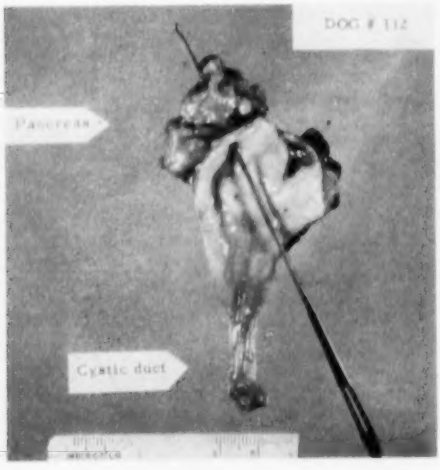
In the six normal control dogs, the gallbladders were blue with thin, translucent walls, and the mucosa was red with delicate trabeculations. Microscopic examination revealed that the gallbladder mucosa consisted of tall columnar epithelium with light-staining cytoplasm and the usual villi; the submucosa consisted of loose fibrous tissue with rare lymphocytes or plasma cells; occasional groups of submucosal glands similar to those seen in the goat's gallbladder were present; the muscularis was slightly thicker than that of the goat, and there were definite subserosal and serosal layers (Fig. 7).

In the seven dogs that were killed three months after pancreaticocholecystostomy, the gallbladders were bluish gray in color and somewhat contracted, with semitranslucent and somewhat thickened walls, and the mucosa was red with coarse trabeculations. Examination of the gallbladders revealed desquamation of the surface epithelium and marked glandular hyperplasia in the mucosa; there was dense infiltration with lymphocytes and plasma cells with obstruction of the outlets of the mucosal crypts, resulting in the formation of cysts containing mucus and exhibiting flattened epithelial lining (Fig. 8); the muscularis was somewhat hypertrophied and infiltrated with lymphocytes. The pathologic interpretation was chronic cholecystitis (Fig. 9).

In the seven dogs‡ that were killed six months after pancreaticocholecystostomy, the gallbladders were gray in color with thick, nonpliable, opaque walls, and the mucosa was dark red with coarse trabeculations. Microscopic examination showed marked glandular proliferation and flattening of the epithelium of the mucosa; the submucosa was densely infiltrated with lymphocytes and plasma cells; there were hyperplasia and penetration of the submucosal glands into the muscularis; the muscularis was markedly hypertrophied, fibrotic, and infiltrated with lymphocytes and plasma cells, and there was dense fibrosis of the serosa and subserosa. The path-

† All the gallbladder specimens were removed while the animals were anesthetized but still living. The gallbladders were immediately incised longitudinally; the bile was removed from them, and within one minute after excision they were placed in neutral formalin solution in order to avoid tissue autolysis.

Fig. 6.—Photograph of the gallbladder and the pancreas in Dog 112 three months after pancreaticocholecystostomy. The probe demonstrates the opening of the major pancreatic duct into the fundus of the gallbladder. (On microscopic examination there was evidence of chronic cholecystitis.)



‡ The pancreas appeared to be normal in three of the seven dogs that were killed six months postoperatively. In the other four animals the pancreas was firm, nodular, and markedly contracted. Microscopic examination of the pancreas in these four dogs revealed marked atrophy of the parenchymal lobules with increased dense intralobular and stromal fibroplasia. There was fibrous thickening of the walls of the major and minor pancreatic ducts without dilatation.

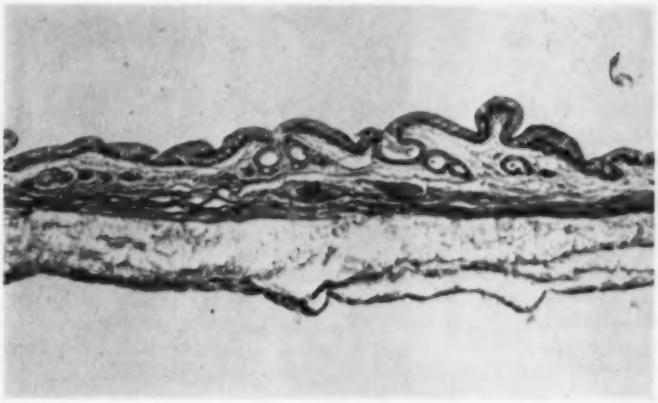


Fig. 7. — Photomicrograph of a section of normal gallbladder of the dog.

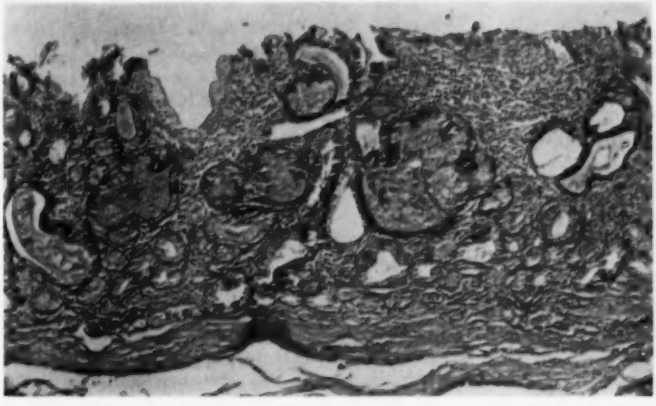


Fig. 8. — Photomicrograph of a section of gallbladder from Dog 73 three months following pancreaticocholecystostomy, showing chronic cholecystitis. This section shows the obstruction of the outlets of the mucosal folds, resulting in mucus-filled cysts with flattened mucosal epithelial lining.

Fig. 9. — Photomicrograph of a section of gallbladder from Dog 78, showing chronic cholecystitis three months following pancreaticocholecystostomy.

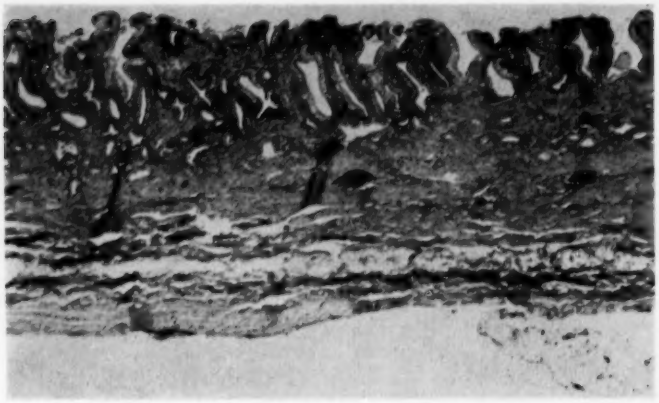


Fig. 10. — Photomicrograph of a section of gallbladder from Dog 85, showing chronic cholecystitis with marked fibrosis six months following pancreaticocholecystostomy.

ologic interpretation was severe chronic cholecystitis (Fig. 10).

Summary

Experimental methods were used to cause pancreatic secretions to pass through the gallbladders of young goats for periods of 6 and 12 weeks and through the gallbladders of dogs for periods of 3 and 6 months. Examinations of these gallbladders revealed increasingly severe degrees of cholecystitis, but no calculi were found.

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REFERENCES

1. Blad, A.: Studien über Gallenperitonitis ohne Perforation der Gallenwege, Arch. klin. Chir. 109: 101, 1917.

2. Westphal, K.: Die durch Dyskinese der Ausführungsgänge bedingten Pankreasfermentschädigungen an den Gallenwegen und der Lober, Ztschr. klin. Med. 109:55, 1928.

3. Wolfer, J. A.: Role of Pancreatic Juice in the Production of Gall-Bladder Disease, Surg. Gynec. & Obst. 53:433, 1931.

4. Butkiewicz, T.: Die gallige Bauchfellentzündung ohne Perforation der Gallenwege, Arch. klin. Chir. 185:55, 1936.

5. Hjorth, E.: Contributions to the Knowledge of Pancreatic Reflux as an Etiologic Factor in Chronic Affections of the Gallbladder, Acta chir. scandinav. (Supp. 134) 96:1, 1947.

6. Bisgard, J. D., and Baker, C. P.: Studies Relating to the Pathogenesis of Cholecystitis, Cholelithiasis and Acute Pancreatitis, Ann. Surg. 112:1006, 1940.

7. Reid, S. E.: Effect of Pancreatic Juice on the Gallbladder, Surg. Gynec. & Obst. 89:160, 1949.

8. Whitrock, R. M., and McCorkle, H. J.: A Practical Method of Anesthesia for Prolonged Surgical Procedures on the Goat, Proc. Soc. Exper. Biol. & Med. 88:221, 1955.

DISCUSSION

ON PAPERS BY DRS. JORDAN AND GROSSMAN; DRS. MENGUY, HALLENBECK, BOLLMAN, AND GRINDLAY, AND DRS. NAJARIAN, HINE, WHITROCK, AND MCCORKLE

DR. ROBERT M. WHITROCK, San Francisco: The etiology and pathogenesis of pancreatitis have been confused since Opie first proposed the common-channel theory. Much of the confusion has resulted from studies that have utilized artificial techniques.

Dr. Najarian is to be complimented on this study, because all this work has been done within the animal itself. It ties in very well with a previous study that was done at the University of California under Dr. McCorkle's supervision, which I should like to illustrate with one slide.

[Slide] In this experiment, also on young goats, the pancreas was again transected and anastomosed to the duodenum. The common bile duct was ligated and transected at the duodenum distal to the junction of the pancreatic and common bile ducts. The results of this experiment revealed (1) acute and chronic cholecystitis; (2) marked dilation and periductal fibrosis of the pancreatic ducts; (3) infection of the bile and mixed pancreatic enzymes obtained from the gallbladder, and (4) no evidence of acute pancreatitis.

We did not know whether the cholecystitis, which was both acute and chronic resulted alone from the presence of mixed bile and pancreatic enzymes in the gallbladder or from stasis of the bile and pancreatic enzymes in the gallbladder with an associated infectious process. The study done

by Dr. Najarian has shown that the cholecystitis required only the mixing of bile and pancreatic enzymes in the gallbladder, without stasis and an associated infectious process.

As to the clinical evaluation of pancreatitis, the question can be raised as to whether one may be dealing with more than one etiologic factor. During the past year we have seen approximately eight cases of what could be termed acute hemorrhagic apoplexy of the pancreas. In this type of case the patient usually gives no antecedent history of pancreatitis. The clinical picture reveals a patient in severe shock that has resisted all types of treatment, resulting in practically 100% mortality.

We think we may have saved one such patient. As Dr. Longmire has previously pointed out, acute hemorrhagic apoplexy of the pancreas may represent a generalized process, similar to the Shwartzman phenomenon. He based his conclusion upon a clinical case in which isolated, aberrant pancreatic tissue revealed the same degree of pancreatitis as the major gland itself.

In contradistinction, we have the other type of pancreatitis, the chronic relapsing form, in which the patient has a long history of misery and pain that is associated with progressive fibrosis and calcification of the pancreas and a low mortality. Surgical treatment has not produced brilliant results, and this brings us to the hope that perhaps in the future we may find a simple method in which we can obliterate the exocrine function of the pancreas and greatly aid the treatment of this group of patients.

Dr. Charles Puestow, Chicago: The three papers on pancreatitis are very stimulating, and I hope that they will be the beginning of a great deal of work that will aid us in a better understanding of this very difficult disease.

I wish to confine my remarks to the paper by Dr. Paul Jordan and his associates, dealing with studies on patients with severe pancreatitis. Their metabolic studies have been meticulous and have revealed very valuable information. I should like to comment on the surgical therapy of chronic relapsing pancreatitis. The operations described by Dr. Jordan, consisting of resection of a portion of the duodenum and varying amounts of the head and body of the pancreas, are formidable procedures and, as Dr. Jordan agrees, are reserved for the advanced stages of chronic pancreatitis. When the disease has reached this stage, it is usually too late to offer much benefit to the patient, who has already become a pancreatic invalid.

Most surgeons agree that in severe acute pancreatitis, which is recognizable without surgical intervention, surgery is contraindicated in most patients and that, when performed, it is directed toward the removal of possible contributory causes, mainly those of the biliary tract. Contrarily, chronic relapsing pancreatitis frequently is treated conservatively until it has progressed beyond the point where operative therapy has much to offer.

Many operations have been recommended for the treatment of pancreatitis. Among these are the Roux-Y type of retrograde pancreaticojejunostomy, described by Duval and also discussed by Dr. Zollinger and his group. In our hands, the retrograde pancreaticojejunostomy has been most satisfactory. We have performed this operation 15 times in the past three years. Our technique consists of mobilizing the tail of the pancreas after removal of the spleen, removing a small portion of the distal end until the dilated pancreatic duct is encountered. Very little pancreas needs to be sacrificed. The jejunum is divided below the ligament of Trietz, and the distal end of the pancreas is inserted into the distal end of the jejunum for a distance of two to three cm. We do not attempt a mucosa-to-mucosa anastomosis. To lessen the possibility of subsequent stricture of the duct opening, a longitudinal incision 0.5 to 1 cm. in length is made in the duct. So far we have had no subsequent stenosis of the duct. This operation permits a free flow of pancreatic juice into the jejunum from the distal end of the gland and also permits some flow into the duodenum if the proximal duct is not completely obstructed.

Of the 15 patients upon whom this operation has been performed, 1 died three months after leaving the hospital. He had returned to his previous habits of excessive alcoholic intake, in which he continued to the time of his death. One patient subsequently developed an obstruction of the common duct due to progression of the disease in the head of the pancreas. Choledochoduodenostomy relieved the jaundice, and the patient has had no subsequent pancreatic symptoms. Most of the remaining patients have done very well, as manifested by weight gain, relief of pancreatic pain, and return of their stools to normal consistency.

These findings lead us to believe that, with the release of intraductal pressure, some restoration of pancreatic function has occurred.

The main purpose of my discussion is to make a plea for earlier surgical therapy for chronic relapsing pancreatitis, so that as much pancreatic function as is possible may be preserved. In our hands the retrograde pancreaticojejunostomy has been the most satisfactory form of surgical therapy.

Dr. Stephen Emmett Reid, Evanston, Ill.: As Dr. Najarian mentioned, in 1948 I did a similar experimental study of the effect of pancreatic juice on the gallbladder of dogs. An experimental procedure was designed to show the effect of pancreatic enzymes on the gallbladder under as nearly physiologic conditions as possible.

[Slide] A segment of the duodenum containing the pancreatic duct was isolated with the pancreas and blood supply intact. The duodenum anastomosis was done to reestablish the continuity of the duodenum. By this procedure the pancreatic juice entered the duodenal pouch in the normal manner, flowed over the gallbladder mucosa, and drained from the cystic duct into the duodenum. The duct of Wirsung in the dog plays a very minor role.

About three weeks later the cystic duct was cannulated, and secretin was injected intravenously. The contents of the gallbladder were collected and assayed for pancreatic juice. Sections of the gallbladder were taken, and the patency of the pancreatic duct was demonstrated.

[Slide] On this slide the specimen has been opened. The duodenal pouch is seen anastomosed to the gallbladder. A probe is shown in the common bile duct, and the anastomosis of the duodenum is demonstrated on this opened specimen.

No pathology was found in 10 dogs subjected to this experiment, but three weeks later the cystic duct was ligated. The dogs became moribund within 100 hours. Sections of the gallbladder, liver, and pancreas were taken.

Six of these dogs showed an acute reaction of the gallbladder, one undergoing complete necrosis. In two dogs acute pancreatitis was demonstrated. Five dogs were found to have fat necrosis of the omentum in the region of the gallbladder. Low-grade peritonitis was found in all 10 dogs. Seven animals had pathologic changes in the liver.

DR. J. DEWEY BISGARD, Omaha: As referred to by Dr. Najarian, several years ago I carried out a series of experiments in goats, utilizing the favorable anatomical factor he has brought out, namely, that the pancreatic duct enters the common bile duct some distance from the duodenum.

[Slide] Thus it is possible to obstruct either the flow of bile only or the flow of both bile and pancreatic secretions, depending upon the level at which obstruction is produced, either above or below the entrance of the pancreatic duct. Permanent obstructions were produced with ligatures; temporary obstructions, by placing a dermal loop around the duct, either above or below the entrance of the pancreatic duct, and bringing it out through a glass tube which was exteriorized on the abdominal wall, so that after a few days the obstruction could be released by simply cutting and removing this dermal loop.

This procedure was carried out in two series of animals. The one I can speak of as the infant series were kids one month or less of age. The others were 5 or 6 months of age or older.

[Slide] This is the appearance of a normal gallbladder in the kid goat and will serve for a comparison.

[Slide] This is a gallbladder after obstruction above the level of the entrance of the pancreatic duct. These gallbladders became distended. Some of them then would recede to normal, after having been obstructed as long as four or five days. Others would go on and develop a chronic cholecystitis, and in these we were able to recover microorganisms from the gallbladder or its wall. With obstruction below the level of the entrance of the pancreatic duct, all infant goats died irrespective of the duration of the obstruction. They died rapidly with gangrenous cholecystitis, often with a good deal of bile in the abdomen; some of them died with hemorrhagic pancreatitis, and others also with liver abscesses.

[Slide] This one shows the pancreatic necrosis.

[Slide] Here are liver abscesses.

[Slides] Most of the older goats survived the period of obstruction and went on to develop this picture of chronic cholecystitis. Next is the same gallbladder laid open, showing the thick-walled gallbladder, the cystic duct, and the much-dilated common duct. Here is to be seen the entrance of the pancreatic duct into the common bile duct, and here, the entrance of the common duct into the duodenum.

[Slide] Three animals developed stones. Two of them had small ones, like the ones above, and one developed large stones, as well as small ones.

DR. PAUL H. JORDAN JR., Los Angeles: I should like to express my appreciation to Dr. Puestow for his contribution to this paper. The results he has reported are very encouraging. They are similar to those that have been reported by Ellison and Duval. When results as good as theirs are obtained with any treatment for this otherwise discouraging clinical entity, we are obligated to reevaluate our thinking about it.

I feel that we are not in conflict with Dr. Puestow's point of view. Ideally, it would be hoped that some suitable operation, perhaps caudal pancreatectomy, could be employed earlier in the disease process, before architectural destruction has progressed to the degree that we feel more radical treatment is indicated.

DR. RENÉ B. MENGUY, Rochester, Minn.: In order to correlate our study of duct obstruction with more physiologic data, we undertook a parallel series of experiments in which we studied pressures in pancreatic and common bile ducts of dogs.

Polyvinyl tubes were placed in these dogs. It will be noted that the sphincter mechanisms of the ducts are resected, so that we obtained truly physiologic interductal pressures. We studied the effects of various drugs, meals, and so on. I want to show you a few slides.

[Slide] It has often been objected that duct obstruction should not be retained as a cause of acute pancreatitis because autopsy studies have only fre-

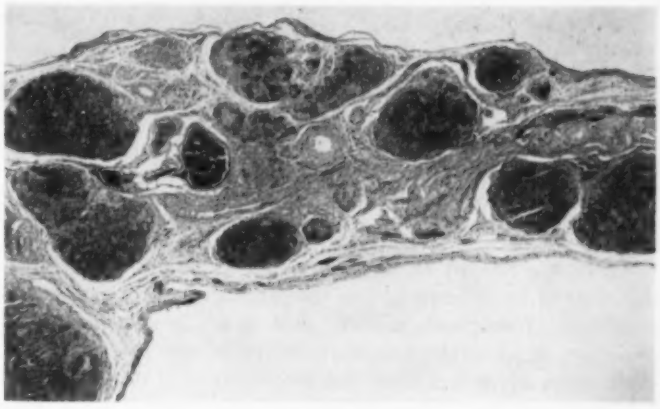

Fig. 11. — Photomicrograph of a section of pancreas, showing parenchymal atrophy and intra- and interlobular fibrosis.

quently revealed an organic cause of obstruction, such as one at the papilla.

Note here the injection of morphine. The duodenal muscle around the pancreatic duct has caused the pressure in that dog duct to attain levels approximating the maximal secretory pressure for prolonged duration.

[Slide] It has often been suggested that a reflux of bile is the cause of pancreatitis. Now, in this duct an animal having gallbladder-duodenal spasm, reduced by injection of morphine, produced a greater degree of rise in pancreatic pressure against almost no change in the biliary pressure.

Actually, perhaps one of the reasons for pancreatitis is that the pancreatic ducts do not have a pressure-regulating mechanism, such as the biliary tree has in the gallbladder, and that is why pancreatic interductal pressure is more susceptible to changes in the tone of the surrounding duodenum.

[Slide] I perhaps should not bring it up at this meeting, but we found that the interduodenal injection of alcohol (40% ethyl alcohol injected into the duodenum) produced a rise in pressure for prolonged periods of time, and this may explain the relationship between alcoholism and acute pancreatitis.

DR. JOHN S. NAJARIAN, San Francisco: There is one further point that I should like to mention at this time. We did not want to enter into a discussion of pancreatitis in this paper, but an interesting pathologic picture occurred in the pancreases of four of the seven dogs in which the pancreatic ducts were anastomosed to the fundus of the gallbladder. The pancreases were markedly contracted, firm, and nodular on gross examination. Microscopic examination revealed definite parenchymal atrophy and intra- and interlobular fibrosis. There was no dilatation of the pancreatic ducts, indicating that the underlying etiology of this pathologic change was probably not secondary to obstruction of the major pancreatic duct. The pathologic interpretation was chronic relapsing pancreatitis.

[Slide] In an effort to explain the apparent differences in our results from those of Dr. Bisgard, who concluded that pancreatic ferments alone, without biliary stasis, would not cause inflammation of the biliary tract, I suggest that the discrepancy may be due to the shorter periods of exposure of the gallbladders to pancreatic ferments in Dr. Bisgard's experiments. In his series of three goats with cholecystostomies and ligation of the common bile duct below the entrance of the pancreatic duct, none of the goats survived beyond eight days. It was because of this finding that we felt that an experiment in which we would be able to study the effect of pancreatic secretions on the gallbladder for a longer period of time would make the comparison with the clinical disease more accurate.

Neoplastic Disease of the Spinal Extradural Space

A Review of Fifty Cases

JOHN MULLAN, M.D., and JOSEPH P. EVANS, M.D., Chicago

When the therapy of an illness falls as far short of the ultimate as does the surgical treatment of neoplastic disease, then it is necessary to reconsider frequently the principles upon which it is based and the results which it achieves. These results are twofold, curative and palliative, and, while our efforts are directed toward the former, we realize all too frequently that the best results will sometimes lie in palliation. The disappointment in accepting this lesser goal must not allow us to underestimate its importance or neglect the help that it may give.

Probably nowhere should palliation have a greater place than in malignant disease of the spinal extradural space, where a relatively simple surgical procedure might be expected to relieve pain and avert the catastrophies of paraplegia, bedsores, and incontinence. Within these limited aims the results should be good; yet this apparently is not the case. Rowbotham [1] speaks of the results being "so disappointing," while more than half Alexander's [2] patients were already paraplegic on arrival at his department. Mann,[3] in discussing Hodgkin's disease, states "death may occur—from paraplegia, for example, following spinal compression."

Such depressing reports led us to reexamine current and previous records at the University of Chicago Clinics of patients who had had laminectomies in the treatment of spinal extradural neoplasm.

A wide variety of tumors was encountered, both malignant and benign. Of the 50 under consideration, 14 were local tumors in that they arose primarily in the spinal extradural space, in the bone, or spread into the extradural space through the intervertebral foramina from the chest. Of the remainder, 15 were reticular tumors and 21 were metastatic. They are listed in Table 1. In spite of many differences, the common location and their similar problems in diagnosis and treatment lead one to discuss these tumors as a group. Tumors arising primarily from the dura mater or nerve roots are not included.

In no instance was surgery alone regarded as curative, though several patients have probably achieved permanent cure with the help of radiotherapy. This report does not, therefore, deal with the length of survival but rather with relief or prevention of spinal cord symptoms within the natural evolution of the disease. Of these 50 cases, 6 had a second operation, that is, a total of 56 procedures. In 16 the results were regarded as good or excellent. These patients recovered from their neurological deficit before or within a reasonable period of leaving the hospital and remained symptom-free and often gainfully employed for the greater part of the life expectancy of their disease. In 13 there was a very considerable improvement, but the patients continued to have some symptoms or neurological deficit, or else the period of survival was disappointingly short. A few returned to some form of work. In seven there was little substantial improvement, but the course toward paraplegia was arrested sufficiently long to regard the operation as having been worth while. There were 14 for whom the operation conferred no benefit. Failure depended upon the malignancy of the disease, degree of neurological

From the Division of Neurological Surgery, University of Chicago Clinics.

Read at the 64th Annual Meeting of the Western Surgical Association, Cincinnati, Nov. 30, 1956.

TABLE 1.—*Summary of Fifty Cases of Spinal Extradural Tumor Treated by Laminectomy and Radiotherapy*

Case No.	Disease	Site *				Function †				Recovery ‡			
		C	T	L	S	1	2	3	4	A	B	C	D
	Local tumors												
1	Hemangioma			1			x			x			
2	Hemangioma		8				x			x			
3	Hemangioma		5				x			x			
4	Hemangioma		5				x			x			
5	Hemangioma		3,4				x			x			
6	Hemangioma		8,9				x			x			
7	Hemangioendothelioma		4–7			x				x			
8	Hemangiopericytoma		6–11				x				x		
9	Hemangiopericytoma		9,10			x							x
10	Giant-cell		11						x				x
11	Giant-cell		10				—		x		x		—
12	Chondrosarcoma		7,8				x					x	
13	Osteogenic sarcoma		8–10				x				x		
14	Myxoliposarcoma		5,6				x			x			
	Reticular tumors												
15	Hodgkin's disease		9						x				x
16	Hodgkin's disease		2,10				x			x			
17	Hodgkin's disease	5-2					x				x		
18	Hodgkin's disease		11,12				x				x		
19	Myeloma	4,5							x				x
20	Myeloma	7-1				x							x
21	Myeloma		9,10,11				x			x			
22	Multiple myeloma				1	x				x			
23	Multiple myeloma		7,8						x				x
24	Lymphosarcoma		10					x			x		
25	Lymphosarcoma		6–8					x				x	
26	Lymphosarcoma		7						x	x			
27	Lymphosarcoma	6						x		x			
28	Reticulin-cell sarcoma		2						x				x
29	Reticulin-cell sarcoma		2–5					x		x			
	Metastatic tumors												
30	Breast		2–6					x—			x		—
31	Breast	5-7					x				x		
32	Breast		4,9				x						x
33	Breast		2–4			x				x			
34	Breast		5,11,12			x					x		
35	Kidney		5					x—					x—
36	Kidney			2–5			x					x	
37	Kidney		12				x				x		
38	Kidney		12			x							x
39	Prostate		7				x		—				x—
40	Prostate		10				x				x		
41	Prostate		7				x				x		
42	Lungs			2			x						x
43	Lungs			5			x						x
44	Thyroid	4-7					x			x			
45	Uterus		8						x			x	
46	Colon		7				x	—				x—	
47	Adenocarcinoma			4-5			x	—			x		—
48	Adenocarcinoma		7				x					x	
49	Mucous adenocarcinoma			4-5			x					x	
50	Melanoma		8					x					x

* C, cervical or cervical thoracic; T, thoracic; L, lumbar; S, sacral.
† 1, no paralysis; 2, moderate paralysis; 3, paralysis almost complete; 4, paralysis complete.
‡ A, good result; B, moderate result; C, fair result; D, failure; X, 1st operation; —, 2d operation.

damage before operation, and, lastly, upon the surgical judgment and skill employed in the management of each individual case.

Relationship of Results to Pathological Nature of Disease

A. Local Tumor Invading the Bone and Extradural Space.—Hemangiomata: There were six of these. All were treated by decompressive laminectomy and postoperative radiation. All had signs of moderate to severe cord compression. All made excellent recoveries.

Hemangioendothelioma: One patient who was operated on because of pain had good relief but died within a year of a cerebral glioma.

Pericytoma: Two examples were encountered. These tumors presumably arise from the Rouget cells of the capillaries, and when there is histological difficulty in differentiating them from the hemangioendotheliomas this can be facilitated by the reticulin stain, which shows the peripheral situation of the cells. Patient 8 had a previous complicated neurological history. He had severe

residual motor weakness from an undiagnosed complete paraplegia which had occurred about six years previously. Laminectomy at that time had had no effect. On this occasion a cuff of pericytoma was removed from T 8 to T 10. He was given x-ray therapy and became ambulatory but now, one year later, has again deteriorated.

The tumor in Patient 9, though not greatly different histologically, grew with extreme rapidity in the chest and extended with finger-like processes into the extradural space. The total duration of this man's illness was about a year. The tumor in both these cases possessed a much more rapid growth than was to be expected from the histological appearance.

Giant-Cell Tumor: There were two of these. Like the hemangiomata, they are locally destructive but do not metastasize. Cures have been reported spontaneously after compression fracture; many other cases have been cured by radiotherapy; biopsy has been said on occasion to accelerate the growth of the tumor (Guri).[4] Both our cases were failures. One (Patient 10) was seen too late, after four months' delay. The other (Patient 11) delayed admission until a compression fracture occurred. Her case will be discussed later in greater detail.

Other Local Tumors: Two patients, one with osteogenic sarcoma and another with chondrosarcoma, had some relief, while one with myxoliposarcoma, who had two thoracic operations and one spinal operation since diagnosis of his condition, 13 years previously, is still at work and symptom-free.

B. Reticular Tumors.—Hodgkin's Disease: There were four cases, improvement being obtained in three.

One (Patient 17) of these had had the diagnosis established 15 years previously and during the interval had had many courses of radiation to enlarged nodes. She survived her laminectomy neurologically well for a further three years. In Patients 15 and 16, the first evidence of their disease was cord compression.

Myeloma: These were a disappointing group. Three cases were single; two were multiple. Of the single cases one (Patient 19) died a few hours after operation. Another (Patient 20), who became quadriplegic during or immediately following surgery, died 18 weeks later. In both these the lesions were cervical. Patient 23, with multiple spinal lesions, had irreversible changes on admission. There are, however, two good results. Patient 21 made a good recovery in spite of further angulation of his thoracic spine and is still at work, five years later. Patient 22, with multiple spine lesions, is also at work, almost two years later. On the whole, however, better results might have been anticipated in this radiosensitive group.

Lymphosarcoma: By contrast, four cases of lymphosarcoma did surprisingly well. One, who was completely paralyzed for 2 months, remains almost symptom-free 20 years later. Patient 24 did reasonably well for 11 years, while Patients 25 and 27 also improved, but the survival was considerably shorter.

Reticulum-Cell Sarcoma: Of the reticulum-cell sarcomata, one case (Patient 28), who was completely paralyzed on admission, made no improvement but the other (Patient 29) made a good immediate recovery, though he died relatively soon afterwards.

C. Metastatic Tumors.—Of 21 cases of metastatic tumor, 5 had two operations—a total of 26 procedures. In two the results were very good. One of these (Patient 32) had pain without any conduction loss, and the other (Patient 44), who had marked weakness from cervical thyroid metastasis, continues well almost two years after decompressive laminectomy and treatment with radioactive iodine. In seven the results were good. In five they were worth while. There were 11 failures, or 7 if we eliminate those second operations undertaken when reasonable hope might have been abandoned.

TABLE 2.—*Degree of Recovery with Incomplete Paralysis*

Case No.	Disease	Duration of Illness, Mo.	Duration of Severe Paralysis,* Days	Duration of Complete Paralysis	Degree of Recovery
27	Lymphosarcoma	18	84	.....	Good
30	Carcinoma of breast	20	30	.....	Nil
25	Lymphosarcoma	12	16	.....	Poor
46	Carcinoma of colon	2	14	.....	Poor
50	Melanoma	15	4	.....	Nil
47	Adenocarcinoma	9	6	.....	Nil
24	Lymphosarcoma	7	1	.....	Fair

* Duration of severe paralysis is judged by date from which patient became confined to bed.

Relationship of Results to Degree of Paralysis at Time of Operation

It is generally assumed that if any power or sensation whatsoever remains before decompression the outlook is much better than in cases of complete functional loss. Patients were divided, therefore, into those who had complete loss, those in whom some minimal conduction could be detected, a larger group with moderately severe paralysis, and a few who presented with pain only. In this series the 7 cases in whom some function was present were only slightly better than those 11 with total loss. Of the former, four were benefited; of the latter, three. The number of successes is too small to equate easily with either the total duration of the illness or the speed of development of the paralysis as indicated by the time that had elapsed between inability to stand and complete functional loss. The relationship is given in Tables 2 and 3.

Of those totally paralyzed, there was a moderately good result in Patient 8 (giant-cell tumor), operated upon after two and one-half hours of complete functional loss. In a single instance (Patient 45), at 12 hours no useful motor recovery was evident but there was a good sensory return, which spared this obese diabetic woman the possibility of bedsores and allowed her to sit up at home in a wheel chair with reasonable comfort. She already had had a lower limb amputation because of diabetic gangrene. Patients operated on at 1, 3, 3½, 6, 30, and 70 days were not improved. But there was one excellent result after 60 days of complete motor and sensory loss, and this case is worth citing in some detail.

CASE 26.—In July, 1935, a woman had a severe pain between her shoulders, following some heavy manual work. By September, this returned and was followed by difficulty of balance. Toward the end of October she felt numb to her axillae, and by Nov. 6 she was unable to walk. On Nov. 10 she had total motor, sensory, and sphincter paralysis. On Jan. 14, 1936, Dr. Bucy removed a rather posteriorly placed tumor which was histologically regarded as a lymphosarcoma. She then had a course of deep x-ray treatment. A year later she returned to work and continued to teach school and do her own housework until her retirement, in 1954. Her residual disabilities have been stiff legs and occasional incontinence of urine.

The Effects of Procrastination in Cases Not Yet Paraplegic

Apart from the unavoidable cases who were seen too late, there were six whose condition deteriorated after they were first

TABLE 3.—*Degree of Recovery with Complete Paralysis*

Case No.	Disease	Duration of Illness, Mo.	Duration of Severe Paralysis	Duration of Complete Paralysis	Degree of Recovery
23	Multiple myeloma	18	110 days	70 days	Nil
26	Lymphosarcoma	6	6 days	60 days	Good
7	Giant-cell tumor	26	120 days	30 days	Nil
28	Reticulin-cell sarcoma	½	Few hr.	6 days	Nil
15	Hodgkin's disease	2	2 days	3 days	Nil
39	Carcinoma prostate	4	Few hr.	3 days	Nil
35	Hypernephroma	5	Few hr.	3 days	Nil
35	Hypernephroma	5	Few hr.	1 day	Nil
45	Carcinoma of uterus	1	5 days	12 hr.	Poor
19	Myeloma	1½	Few hr.	3½ hr.	Nil
8	Giant-cell tumor	5	1 hr.	2½ hr.	Fair

seen in hospital. A near failure was Case 27 (lymphosarcoma). He complained of shoulder pain for one and a half years and numbness together with weakness of his hands for one week. There was radiological bone alteration at the seventh cervical vertebra. Following lumbar puncture, quadriplegia developed over a period of three days. Operation was deferred, because of a cold, but the paralysis became practically complete and included the respiratory muscles. He was placed in a respirator and operated upon without further delay, and he was eventually able to walk out of hospital. This is the only case in the series in which a lumbar puncture probably hastened paralysis, but such a possibility, especially in the cervical region, is too well known to justify the procedure in these cases outside of a neurosurgical center.

Case 11.—A woman had a giant-cell tumor, complained of backache and was seen to have destruction of the 10th thoracic vertebra. She was advised to enter the hospital but insisted on returning home to take care of her children. Eleven days later, when picking up a child, she had an excruciating pain. This increased over two days, and she was admitted with an over-distended bladder and some hyperalgesia of the feet, but good motor power. While she was being x-rayed, power deteriorated, and at the end of the procedure it was absent. The 10th vertebra was now seen to be collapsed. Decompression was done within two and a half hours of her complete paralysis, and she was later given deep x-ray treatment. Her recovery was fairly good, but within two years her condition again deteriorated. Exploration now revealed no tumor, and from the site of collapse an extensive angulating hyperostosis was removed. She has remained paralyzed since.

It is most likely that this patient's vertebra collapsed when she was picking up her child, but it is certainly possible that manipulation on the x-ray table contributed to the collapse. This emphasizes that we must regard an infiltrated vertebra as a potentially fractured vertebra and that even a relatively benign extradural lesion, such as a giant-cell tumor, must be treated with great respect and without delay.

Case 35.—A lawyer with hypernephroma and incipient paralysis had to return to his urgent law practice but was readmitted 48 hours later, having by that time been completely paralyzed for 24 hours. He had pain in his arm with wasting of the small hand muscles, and, though his sensory level was lower, the region corresponding to the disability was explored without delay and without myelography because of the severity and urgency of his compression. This was the wrong level. A subsequent decompression was made at the correct site (T 5), but he made no recovery.

There were others. Patient 19 (with myeloma) walked into the hospital and became completely paralyzed the same day. He was operated upon within 24 hours, but he died three hours later. At autopsy there was evidence of coronary insufficiency, but whether this was the predisposing or final cause of death is uncertain.

The condition of Patient 39 slowly deteriorated and was unrelieved by two operations. Patient 45, the diabetic already referred to, became paralyzed while her blood sugar was being standardized.

In none of the six patients whose condition deteriorated after they were first seen at hospital was the delay without serious significance. One died; three remained paralyzed; two made tardy recoveries. One of these later again relapsed and is also a permanent paraplegic.

In short, diagnosis must be early and treatment immediate. Of 18 operations where paralysis was complete or nearly so, good results were obtained in 2, reasonable improvement in 2, and minimal improvement in 3. No recovery took place in 11. Of 38 other operations there were good results in 14; 11 were improved, 5 were regarded as having been worth while, and only 8 were regarded as failures.

Other Causes of Failure

Patient 42, with carcinoma of the lung, died of shock on the day following operation, in spite of apparently adequate blood replacement. At autopsy it was found that his adrenals were completely destroyed by tumor.

Patient 38, an addict, was not relieved of pain by decompression of his tumor or by bilateral cordotomy, even though an

apparently satisfactory level of analgesia was achieved.

Patient 11, who had pericytoma, diagnosed at a previous chest exploration, had his spinal pain treated by root section. This was only temporarily satisfactory. The result was short-lived, as tumor continued to extend into the spinal canal through other intervertebral formina. It was later more effectively controlled by radiotherapy, which, in retrospect, should have been the initial treatment.

Diagnosis in Spinal Extradural Tumors

In the absence of previous evidence of reticular or metastatic disease, the diagnosis of the exact type of extradural compression is not easy. While an insidious onset is commoner with a relatively benign lesion, this is not necessarily true, and the converse may hold. For example, Patient 35, who had carcinoma of the kidney, had pain for about 5 months, while Patient 6, who had a hemangioma, had trouble for only 10 days. In a few instances, for example hemangiomata, the x-ray appearance may be diagnostic, but in the majority of cases the appearance is either normal or else there it a nonspecific bone erosion, often involving laminar pedicles. The cerebrospinal fluid manometric studies are helpful in deciding whether there is severe compression. They are less useful in deciding the degree of danger from incomplete compression. The amount of protein alone in the fluid does not help greatly, cases with complete myelographic block occasionally having a figure as low as 50 mg. per 100 cc. Except in instances of very long-standing compression, few were over 500 mg. per 100 cc. A figure greater than this is more commonly found with intradural tumors and more particularly with the intramedullary group and the neurofibromata than with the meningiomata. If a block is incomplete, the amount of protein is of little help in differential diagnosis.

Management of a Patient Without Paraplegia

Whether the tumor is primary or secondary, it should be dealt with at once. If it is secondary, then radical cure is out of the question and the delay involved in extensive investigation of an elusive yet symptom-free primary lesion may jeopardize the chances of favorable palliation.

1. In the case of suspected tumor without radiological change in bone, the situation of the presumed tumor should be checked by myelography. Speculative radiotherapy has no place.

2. With bone destruction, in the absence of neurological and myelographic signs of compression, radiation therapy may be given a trial.

3. In all undiagnosed cases with evidence of compression, a laminectomy will afford diagnosis and give relief from pressure. If this is not done, it would be possible to irradiate a resistant tumor or even such a lesion as a completely prolapsed lumbar disc, which has been known to mimic extradural malignant disease.

4. When the diagnosis of a radiosensitive tumor has already been made, e. g., in a known case of myelomatosis, if the neurological signs of compression are mild even though there is complete myelographic block, radiation may be given under careful supervision. If the neurological signs are marked, then decompression is indicated before radiation therapy.

The best method of treating the radiosensitive tumors is still open to question, as, for example, in the case of hemangiomata. The relative merits of surgery and radiation have, in this particular instance, been debated over the years. The surgical mortality, because of hemorrhage, was previous to 1930 stated by Bucy [5] to be 60%. Twelve years later, Ferber and Lampe [6] gave a figure of 20% and stated that a further 10% were not improved. Of 14 cases treated by therapy alone, 10 made perfect recoveries; in 3 the result was almost satisfactory, and only in 1 was surgery required

because of progression. Progression, however, does occur. Guri mentions a case in which a cervical hemangioma progressed in a similar manner. In our experience and that of others, the cervical area is probably an especially dangerous situation for extradural tumors. The excellent results of the present series favor immediate decompression followed by radiation. Hemorrhage may certainly be a problem. In Freedman's [7] case this was overcome by staging the operation in three separate procedures.

Management of a Patient Already Paraplegic

Tarlov's [8,9] work suggests that the mammalian spinal cord has considerable power of recovery from total paralysis of gradual onset, dogs paralyzed over a period of 48 hours having recovered when decompression was done one week later. He further confirms this impression in a series of nine human cases of intradural tumor who made variable degrees of satisfactory recovery after periods of complete paralysis ranging from two weeks to six months. This potential is, unfortunately, not realized with extradural tumors. There are a number of reasons. In the first place, the tumor is rarely removed completely, because it is anteriorly placed and because it is vascular. Angulation due to collapsed vertebrae and extrusion of intervertebral disc substance will continue to act as a source of pressure after the decompressive laminectomy. More important is tumor regrowth, which causes new compression before there is time to recover from the old, and this is the factor which distinguishes the radiosensitive from the radioresistant tumor. Nevertheless, our single experience of useful recovery following compression of two months' duration encourages effort even in apparently hopeless cases.

Treatment of Pain

Many patients who have had good motor and sensory improvement continue to complain of pain, and some, especially those with collapsed vertebrae, may be bedridden because of it. Rhizotomy might seem to be a reasonable answer, but we have been reluctant to open the dura and allow the more easy access of tumor tissue to the unprotected cord. This is not, perhaps, a valid contraindication. Three patients have had rhizotomy. In two of these the results were temporarily good. In one there was some improvement.

Cordotomy has been little used in these cases, partly because so many of the lesions are high thoracic ones that a satisfactory bilateral analgesic level would be difficult to achieve. A more important objection is that slight impairment of motor conduction resulting from the cordotomy might be more than an already damaged cord could stand.

One patient (Patient 33) was referred for possible cordotomy because of intractable pain from secondary breast carcinoma of the upper thoracic spine. She was found to have a complete myelographic block, though there were no neurological signs. Simple decompression and subtotal removal of the tumor gave her very adequate relief from pain.

Role of Radiotherapy

In practically all these cases, deep x-ray therapy was given postoperatively, and to this in a large measure must be attributed the good results. Radiotherapy alone for the treatment of pain was tried preoperatively, with temporary success in three of these cases. Radioactive iodine has been of marked help in one patient with a radiosensitive cervical secondary tumor from her thyroid. She recovered from a moderate paraplegia following decompressive laminectomy and administration of 500 mc. of I^{131} and remains well almost two years later.

Summary and Conclusions

Fifty cases of spinal extradural tumor treated by laminectomy and postoperative radiotherapy are presented; six had two operations.

TABLE 4.—*Summary of Results*

Results, %			
Good	Moderate	Fair	Failure
32	26	14	28

Causes of Failure in 19 Cases			
Delay	Poor Selection	Poor Technique	Combined Factors
11	3	2	3

Causes of Delay			
Not referred in time, total	5	Diabetes	1
Family reasons	1	Cold	1
Business reasons	1	Unstated	2

Percentage of failures if these avoidable delays had been eliminated would have been approximately 10%

Good results were attained in 32%; 26% were moderately improved, and in 14% the result was worth while; 28% were failures.

Causes of failure were degree of malignancy, degree of cord damage before treatment, and errors of judgment and of technique.

Best results were obtained in the simpler radiosensitive tumors; next most favorable were the reticular tumors, and least favorable were the metastatic neoplasms.

Investigation, preferably by myelography, of each case of suspected spinal extradural tumor is urged. In cases of unknown histology radiotherapy may be given under close neurological observation where myelographic block is incomplete. If the pathology is known and the tumor is radiosensitive, radiotherapy is given, provided that pressure on the cord is minimal. In all cases when compression is present and the tumor is insensitive to x-rays or when the diagnosis is unknown, or even in radiosensitive tumors where there are marked neurological signs, urgent decompression and postoperative irradiation are indicated. In the presence of spinal cord involvement, the need for operation is urgent and time must not be wasted in prolonged investigation of a suspected primary lesion.

In the presence of complete paraplegia it is difficult to say when it is too late to offer help, as we have had one good result after two months of paraplegia.

In no instance was a satisfactory result achieved by a second operation.

If all cases had been referred to hospital before paraplegia was established, the percentage of failures would have been 18 instead of 28. If, in addition, all those referred with evidence of extradural tumor but without paraplegia had been operated on immediately upon admission, that figure would have been no more than 10%; a higher figure seems hardly permissible under present-day conditions and should be reduced still further.

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REFERENCES

1. Rowbotham, G. F.: Early Diagnosis of Compression of the Spinal Cord by Neoplasms, Lancet 2:1220, 1955.

2. Alexander, E., Jr.; Davis, C., and Field, C. H.: Metastatic Lesions of the Vertebral Column Causing Spinal Compression, Neurology 6: 103, 1956.

3. Mann, W. N.: Hodgkin's Disease, Practitioner 177:133, 1956.

4. Guri, J. P.: Tumors of the Vertebral Column, Surg. Gynec. & Obst. 87:583, 1948.

5. Bucy, P. C., and Capp, C. S.: Primary Hemangioma of Bone with Special Reference to Roentgenologic Diagnosis, Am. J. Roentgenol. 23: 1, 1930.

6. Ferber, L., and Lampe, I.: Hemangioma of Vertebra Associated with Compression of the Cord, Arch. Neurol. & Psychiat. 47:19, 1942.

7. Freedman, E.: Hemangioma of the Vertebrae: Diagnosis and Treatment, Clin. Bull. West. Reserve Univ. 4:39, 1940.

8. Tarlov, I. M.: Spinal Cord Compression Studies: III. Time Limits for Recovery After Gradual Compression in Dogs, A. M. A. Arch. Neurol. & Psychiat. 71:588, 1954.

9. Tarlov, I. M., and Herz, E.: Spinal Cord Compression Studies: IV. Outlook with Complete Paralysis in Man, A. M. A. Arch. Neurol. & Psychiat. 72:43, 1954.

Capillary Resistance in Response to Anesthesia and Surgery

Special Reference to Cardiac Arrest

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Recent studies pioneered by Moore and his associates [1] resulted in a rapid progress toward a better understanding of the pathophysiologic changes that develop during surgery and surgical convalescence. Owing to its complexity, the problem has been attacked from many sides: by studying the metabolic and hemodynamic changes, the hematologic response, or the endocrine situation. In our work a new approach has been attempted which may lead to further contribution to this problem. It is based on studies of the capillary resistance.

Previous studies during the last five years have shown that the measuring of capillary resistance is not merely a test for bleeding tendency but is possessive of greater significance. Capillary resistance is subject to endocrine influence.[2,3] Certain corticoids, vasopressin, and oxytocin increase capillary resistance, while the somatotropic hormone decreases it. Histamine also was found to decrease capillary resistance. Capillary resistance shows typical changes following stressful stimuli.[4-6] These changes, termed capillary stress response, are of two kinds, the immediate response, which sets in promptly but lasts only a few hours, and the late response, which appears after a period of latency and is of longer duration. Whereas the late response is connected with the adrenal cortex and, therefore, is abolished by adrenalectomy, the immediate response is independent of the adrenals and seems to be the result of a combined action of vasopressin and histamine.[7]

In connection with anesthesia and surgery the late response was studied and described in a previous publication.[8] The changes occurring after the intervention and during convalescence were found to be related to the amount of tissue involved in the procedure, sex of the patient, and individual characteristics. A protracted late response was encountered when the patient developed complications and especially when his clinical course deteriorated.

The present preliminary paper deals with the immediate response, i. e., with the capillary resistance changes occurring during the surgical intervention.

Method and Procedure

A control level of capillary resistance was determined during a period of five to seven days prior to the intervention; then readings were taken almost continuously during the various phases of anesthesia and surgery. The results are based on 31 experiments in the rat and dog and on 50 observations of surgical patients. The latter were arbitrarily chosen in order to obtain a sampling of as many different surgical procedures and routine types of anesthesia as possible. In the animal experiments the effect of ether, nitrous oxide, and intravenously administered pentobarbital sodium anesthesia were studied alone and in combination. The surgical interventions were standardized—thyroidectomy or hypophysectomy in the dog, sham adrenalectomy in the rat. Capillary resistance was tested in the antecubital area in patients and on the abdominal skin in experimental animals with the negative pressure method, using the electrically or hand-powered apparatus, respectively, devised in this laboratory. Details of

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the method and evaluation of the readings have been described in previous papers.[8,9] Blood studies for the presence of antidiuretic substance were made in 39 animal experiments and in seven patients prior to the intervention and during the immediate stress response with the intravenous rat bioassay method by Jeffers, Livezey, and Austin.[10] In order to determine the nature of the antidiuretic substance, the plasma was also tested for eventual chloruretic property. The chloride concentration in the urine of the test rats was measured by the method of Schales and Schales.[11]

Results

Immediate capillary response was found in 22 patients. In 17 cases capillary resistance increased; in 1 case it decreased, and in 4 cases typical biphasic response developed. In 28 patients immediate response was not observed.

An analysis of these clinical results together with the experimental findings suggested several factors to be decisive as to the occurrence of the immediate response. At this preliminary writing our impressions may be summarized as follows:

1. Immediate response seems not to develop when inhalation anesthesia is preceded by smooth intravenous induction, when anesthesia is well balanced throughout the operation, and when there are no respiratory difficulties. No immediate response was observed during operations with spinal anesthesia.

2. Immediate response practically always occurs when inhalation anesthesia is applied directly without premedication and induction.

3. Immediate response is likely to occur with patients who are incompletely prepared, with inadequate or too rapidly administered induction, and in cases of respiratory difficulty as well as clinical or subclinical anoxia.

4. The type of operation seems not to be decisive. Extensive tissue trauma or bleeding, however, may be conducive to immediate response.

During the immediate capillary response the plasma was found to contain a substance with antidiuretic and chloruretic properties compatible with vasopressin. In one patient, during repair of a diaphragmatic hernia, cardiac arrest developed. Capillary resistance increased markedly (by 20 cm. Hg), and large amounts of antidiuretic substance were found in the plasma. Unexpected cardiac arrest was witnessed in an old, fat, well-trained dog during a study of ether anesthesia. Capillary resistance increased by 15 cm. Hg prior to the accident, and the blood assay revealed large amounts of antidiuretic and chloruretic substance.

Comment

The capillary stress response that develops with anesthesia and surgery seems to be a further item among the many changes that are known to constitute the patient's response to our intervention. In Moore's classification[1] these changes are grouped, according to the underlying factors, as symptoms of the "adrenergic-corticoid phase," those of the "corticoid-withdrawal phase," and those of the "anabolic phase." The adrenergic-corticoid phase is characterized, according to Moore, by a discharge of epinephrine, corticotropin (ACTH), and adrenal corticoids. The fact that immediate capillary response occurs during the first part of this phase (i. e., during and a few hours after surgery) indicates that histamine and vasopressin also play a role in it. Although corticoids are discharged early in this phase, owing to the latent period required for their capillary activity, they do not give rise to a late response until about five hours after the beginning of the intervention. Thus, the late capillary response appears only in the second part of the adrenergic-corticoid phase, but it may extend well into the "corticoid-withdrawal phase," showing a gradual decrease in the capillary resistance to normal or an overshoot decrease in case of a biphasic response.

Even though vasopressin discharge seems to be a common occurrence in stressful situations and may represent a physiologic or borderline-pathologic phenomenon, the possibility that an unusually large concentration of this substance in a particularly

sensitive person may have harmful effects cannot be denied if only its constricting effect upon the coronary arteries and depressing action on the myocardium are recalled. The two observations reported here are certainly suggestive of this possibility. The finding that immediate capillary response occurs only under definite conditions seems to indicate that this apparently undesirable response with its possible dangers may be avoided or minimized.

The number of the present observations does not allow as yet any conclusion as to the practical applicability and use of the capillary resistance test during surgery. In particular, more experience is needed to show whether or not this test is an asset when added to our present armament in the control of the patient's reaction to anesthesia and surgery.

Summary

In continuation of the study of capillary resistance changes developing in convalescence after surgery (late capillary stress response), the changes were investigated that occur during anesthesia and surgery (immediate capillary stress response). Clinical observations were integrated with experimental studies on rats and dogs.

Immediate capillary response was not found if anesthesia was uneventful, with the patient properly prepared, and if during surgery the tissue damage had been moderate and bleeding well controlled. Capillary response was encountered whenever anoxia developed or extensive tissue trauma occurred. The blood of the subjects was found during the immediate response to contain an antidiuretic and chloruretic substance compatible with vasopressin—a finding in conformity with previous studies on the mechanism of immediate capillary stress response. In view of the constricting effect of vasopressin upon the coronaries and its depressant action upon the myocardium, it is conceivable that unusual large concentrations of this substance in a sensitive subject may have harmful effects. Two observations on cardiac arrest seem to support this assumption.

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REFERENCES

1. Moore, F. D.: Bodily Changes In Surgical Convalescence, in Fourth Annual Report on Stress, by H. Selye and G. Heuser, Montreal, Canada, Acta, Inc., 1954, p. 172.

2. Kramár, J.: Endocrine Regulation of the Capillary Resistance, Science 119:790, 1954.

3. Kramár, J.; Meyers, V. W.; McCarthy, H. H., and Simay-Kramár, M.: Further Study on the Endocrine Relations of Capillary Resistance, to be published.

4. Kramár, J.: Stress and Capillary Resistance, Am. J. Physiol. 175:69, 1953.

5. Kramár, J.; Peetz, D. J., and McCarthy, H. H.: Capillary Response to Emotion, Psychosom. Med. 16:393, 1954.

6. Kramár, J.; Meyer, V. W.; Simay-Kramár, M., and Wilhelmj, C. M., Jr.: Immediate Capillary Stress Response, Am. J. Physiol. 184:640, 1956.

7. Kramár, J.; Meyers, V. W.; McCarthy, H. H.; Dietz, H., Jr.; Simay-Kramár, M., and Williams, J. W.: Mechanism of the Immediate Capillary Stress Response, to be published.

8. Kramár, J.; Peetz, D. J., and McCarthy, H. H.: Trauma and Capillary Resistance, Surgery 35:772, 1954.

9. Kramár, J.; Meyers, V. W., and Simay-Kramár, M.: Contribution to the Physiology of Capillary Resistance in the Human, J. Lab. & Clin. Med. 47:423, 1956.

10. Jeffers, W. A.; Livezey, M. M., and Austin, J. H.: Method for Demonstrating an Antidiuretic Action of Minute Amounts of Pitressin, Proc. Soc. Exper. Biol. & Med. 50:184, 1942.

11. Schales, O., and Schales, S. S.: Simple and Accurate Method for the Determination of Chloride in Biological Fluids, J. Biol. Chem. 140: 879, 1941.

Electrical Ventricular Defibrillation

The Relationship Between Epicardial Burns and Late Mortality

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Ventricular fibrillation was described by Ludwig and Hoffa in 1849,[1] and evidence was offered at the beginning of our current century that successful defibrillation could be achieved chemically or electrically.[2]

The production of cardiac asystole following the coronary perfusion of potassium ions and the reconstitution of a normal vigorous rhythm with calcium has been well described in both normothermic and hypothermic preparations.[2-4] There has been a lack of universal acceptance of this method of defibrillation among cardiac surgeons, largely because ventricular fibrillation tends to recur following the coronary perfusion of calcium.

Electrical shock, conversely, enjoys considerable popularity as the means of reverting ventricular fibrillation to a normal sinus rhythm. The precise manner of application has undergone constant constructive revision.

Our own specific interest in this subject evolved from recent attempts to prevent ventricular fibrillation during open cardiotomy with use of hypothermia. In these studies it became evident that the application of those defibrillating techniques which we had employed in both the laboratory and the operating room were associated with a high postoperative mortality, in spite of the reestablishment of a regular sinus rhythm. A resolution of this paradox was sought.

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Methods

Mongrel dogs, weighing from 6.4 to 16.3 kg., were chosen at random from a large isolation run. The only selection involved was an attempt to exclude those animals which were obviously ill or within the extremes of age. None received any special preoperative diet or therapy. No preanesthetic medication was employed. Pentobarbital sodium was administered intravenously as the anesthetic. The dosage was adjusted to eliminate the lateral canthal reflex with preservation of the medial, which required about 30 mg. per kilogram of body weight. After tracheal intubation, the animals were placed in an ice-water bath, and positive-pressure respiration was begun with 100% oxygen. Removal from the ice-water was done when a rectal temperature of 29 C was reached. A further decline of 3-5 C occurred, so that the following procedures were performed at a rectal temperature of 24-26 C.

All the animals underwent bilateral transsternal thoracotomy. Right ventriculotomy was then performed during an inflow-outflow circulatory occlusion of from 8.5 to 13.0 minutes.

Various pharmacologic agents (bethanechol [Urecholine] chloride U. S. P., procainamide [Pronestyl] hydrochloride U. S. P. and 2-diethylaminoethylisonicotinamide [Amboneslyl; Mc 4112]) were administered by coronary perfusion to most of these dogs prior to ventriculotomy, in accordance with efforts to prevent ventricular fibrillation under these experimental conditions. The results of these efforts will be reported at a later date.

When ventricular fibrillation did occur, it was allowed to persist throughout the remainder of the predetermined period of circulatory occlusion. Defibrillation was attempted as follows:

1. Epinephrine, 1.0 ml. of a 1:10,000 solution, was injected into the right auricle or ventricle. In those animals which had received bethanechol, intracoronary atropine sulfate was used rather than intracardiac epinephrine.

2. Intermittent manual cardiac compression was performed for 1 minute to perfuse the brain, followed by an additional 30 seconds of compression with the aorta occluded distal to the coronary ostia to selectively perfuse the myocardium.

3. Electrical defibrillation was attempted by applying single or coupled shocks of 170 or 220 volts for 0.13 or 0.20 second, with bare electrodes (2 in. diameter) placed at the right auricle and cardiac apex.

This protocol of defibrillation was modified during the latter portion of this investigation and, as such, is described later in this report.

"Survival" of the animals was defined arbitrarily as meaning good health seven days postoperatively.

Results

From November, 1955, until April, 1956, there were 30 animals which had undergone hypothermia, bilateral transsternal thoracotomy, and right ventriculotomy. These were divided among four experimental groups, according to the agent or agents which they received to inhibit ventricular fibrillation, i. e.: bethanechol alone, Ambonestyl alone, Ambonestyl plus bethanechol, and a control group, the members of which received no pharmacologic protection. Evaluation of the mortality within the respective groups immediately suggested a division of the whole series into two broad categories according to whether ventricular fibrillation had or had not occurred at some time during the operative procedure.

Of the 16 dogs which had had fibrillation, defibrillation was achieved successfully in 15, but 11 of these died during the seven-day survival period. This represented a successful defibrillation of 94% but a late mortality of 74%. Of the 14 animals in which there was no fibrillation, all were living and well seven days postoperatively (Table 1).

Originally, we felt that these data supported our impression that ventricular fibrillation, in some way, was deleterious to the myocardium. However, it was postulated that the arrhythmia itself was relatively innocuous and that our standard methods of achieving defibrillation rendered the myocardium incapable of prolonged normal function. Investigation of this latter possibility was begun.

Reflection upon our laboratory and clinical experiences revealed that residual epicardial burns over the lower left ventricle and cardiac apex were present frequently following electrical defibrillation; however, they did not appear to affect normal cardiac function, as the latter was observed during closure of the pericardium and thorax. Nevertheless, steps were taken to prevent similar occurrences in subsequent attempts at electrical defibrillation, i. e., the bare faces of the defibrillator electrodes were covered with saline-soaked gauze sponges, cotton, or felt.

Ten dogs developed ventricular fibrillation during the further course of these same experiments. In all defibrillation was successful with one or two shocks of 220 volts applied for 0.13 second, with the electrodes protected as described. Of these, 9 * were alive and well one week postoperatively, a late mortality of 10%. Such results compare favorably with the group in which no fibrillation occurred (Table 2).

In each of the cases in which the ventricles were defibrillated with padded electrodes, the heart was inspected carefully for epicardial burns before the pericardium was closed. Of these, nine revealed no gross evidence of burn or contusion. In one, the

TABLE 1.—*Comparative Late Mortality of Dogs Defibrillated with Unpadded Electrodes*
November, 1955-April, 1956

Group	No.	Died	Mortality, %
Defibrillated with unpadded electrodes	15	11	74
No Fibrillation	14	0	0

* The one death in this group resulted from an overdose of barbiturate prior to bronchoscopy on the first postoperative day.

TABLE 2.—*Comparative Late Mortality of Dogs Defibrillated with Padded Electrodes*

Group	No.	Died	Mortality, %
Defibrillated with unpadded electrodes (November, 1955–April, 1956)	15	11	74
Defibrillated with padded electrodes (April, 1956–September, 1956)	10	1*	10
No fibrillation (November, 1955–September, 1956)	20	0	0

* Death due to overdose of barbiturates prior to bronchoscopy on first postoperative day.

first of the series, the moistened gauze sponges were held in place over the electrode faces by two crossed rubber bands. A small (4 by 4 mm.) cruciate burn, which was well tolerated by the animal, was noted over the cardiac apex and corresponded to the intersection of the rubber bands. Subsequently, the padding was held in place by cotton tapes.

Early microscopic examination of electrically burned areas disclosed basophilia of the myocardium and foci of interstitial hemorrhage. Later changes in areas of electrical shock have been studied by Tedeschi and White[5] and include myocardial necrosis, fibrosis, and fragmentation.

Comment

During the evolution of present techniques of electrical ventricular defibrillation, certain features have come to be recognized as essential to ultimate success: (1) adequate pulmonary ventilation and respiration; (2) effective intermittent cardiac compression, to prevent tissue hypoxia, particularly of the brain and heart[6]; (3) the preservation of myocardial tone capable of maintaining an adequate systemic circulation once a regular rhythm has been regained[7,8]; (4) regular auricular contractions to assure a pacemaker for the ventricles in the immediate postdefibrillatory period[7,8]; (5) simultaneous depolarization of the entire ventricular myocardium by electrical means.[7]

Specific techniques have been perfected within each of these rather broad categories, which, subtle as they may appear at first, may be crucial in any given case.

Cardiac compression itself is a maneuver which requires considerable practice to attain that quality of cardiac ejection which will maintain an adequate systemic blood pressure without being associated with myocardial contusion[9] or, indeed, penetration. The exact rate of compression has been the object of some controversy.[10-13] It is our feeling that the rate should be influenced by the promptness of diastolic filling, which usually permits 60 to 90 ejections per minute.

Attempts to defibrillate hypoxia ventricles have been found unrewarding universally. We do not apply electric shock unless the myocardium is frankly pink or, preferably, red. These circumstances may be achieved by cardiac compression alone. More frequently, ancillary measures such as intermittent cross clamping of the aorta distal to the coronary ostia, with or without injection of 1.0 or 2.0 ml. of 1:10,000 epinephrine solution into the right side of the heart, are required to assure adequate coronary artery perfusion.

The beneficial effects of epinephrine in setting the stage for successful defibrillation have been stressed by Senning[8] and others[12,14-16] and have been corroborated by us. These include improvement of coronary perfusion by coronary vasodilatation and increased peripheral resistance, improvement of myocardial conduction, and stimulation of the origin of impulses in the right auricle. We agree with those who feel that epinephrine does not appear to predispose to subsequent ventricular fibrillation when it is properly employed in the defibrillating regimen.

Electrical ventricular defibrillation occurs when the entire ventricular myocardium is depolarized. This may be achieved by the passage of currents of 1.0 amp. or greater through the heart from side to side or from base to apex.[10,17] Smaller currents are usually unsuccessful or may even serve as stimuli to fibrillation.[14,18] Within the effective range (1.0 amp. or greater) smaller currents, as represented by potential differences of about 110 volts, usually must be applied in rapid succession to be effective, as in Wiggers' description of serial defibrillation.[19] Presumably, each shock depolarizes progressively greater areas of myocardium until the state of complete depolarization is reached. Larger currents, as represented by potential differences of 220 volts, usually attain this goal following a single brief (0.13 second) application in the nomothermic or hypothermic heart.[14,20] We sub-

scribe to this latter technique, largely because it is expeditious.

Employment of higher voltages increases the possibility of cardiac burns. To prevent these and to improve conduction at the electrode-epicardial interfaces, most of the earlier writers and some of the more recent ones have advocated insulating the heart by applying gauze or some other porous fabric to the faces of the electrodes and soaking this insulator with saline prior to delivery of the electric shock.[11,13,14,17-19,24] However, coincident with the advent of our present era of cardiac surgery and the employment of higher defibrillating currents, many treatises have overlooked this item.[3,8,10,12,15,16,20-23]

Few commercially available defibrillators with which we are acquainted are furnished with a means of insulating the electrode faces or, indeed, carry the recommendation that such a technique be employed. This is perhaps unfortunate, in view of the evidence offered here that the prevention of cardiac burns may be essential to a satisfactory clinical course following successful ventricular defibrillation.

Summary and Conclusions

The survival of animals undergoing transsternal thoracotomy and right ventriculotomy during hypothermia is presented in its relation to the occurrence of ventricular fibrillation during the operative procedure. A high "late mortality" in those dogs in which "successful" defibrillation was accomplished was considered to result from the method of defibrillation rather than from the arrhythmia itself. A practical technique of ventricular defibrillation is set forth, which emphasizes the importance of avoiding electrical burns and which imposes a low intrinsic mortality.

Although ventricular fibrillation may be relatively innocuous when properly treated, we do not subscribe to the elective production of this arrhythmia during open cardiotomy.[8,25] We believe that a regular sinus rhythm, with or without periods of elective cardiac asystole, is desirable during intracardiac and extracardiac procedures. If ventricular fibrillation should supervene, electrical defibrillation is readily executed. However, the production of myocardial and epicardial burns during this experience may preclude adequate cardiac function in the postdefibrillatory period. Prevention of such burns is achieved by interposing saline-soaked gauze sponge, cotton, or felt between the heart and the defibrillator electrodes. This technique is not new, but its relation to postoperative mortality may not have been appreciated previously.

We recommend that manufacturers of electrical defibrillating devices advise their clients regarding the importance of this facet of the successful application of their product.

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REFERENCES

1. Wiggers, C. J.: Mechanism and Nature of Ventricular Fibrillation, Am. Heart J. 20:399, 1940.

2. D'Halluin, M.: Le Massage du coeur, Presse méd. 12:345, 1904.

3. Hooker, D. R.: On the Recovery of the Heart in Electric Shock, Am. J. Physiol. 91:305, 1929.

4. Swan, H.; Zeavin, I.; Blount, S. G., Jr., and Virtue, R. W.: Surgery by Direct Vision in the Open Heart During Hypothermia, J. A. M. A. 153:1081, 1953.

5. Tedeschi, C. G., and White, C. W., Jr.: Morphologic Study of Canine Hearts Subjected to Fibrillation, Electrical Defibrillation and Manual Compression, Circulation 9:916, 1954.

6. Wiggers, C. J.: Cardiac Massage Followed by Countershock in Revival of Mammalian Ventricles from Fibrillation Due to Coronary Occlusion, Am. J. Physiol. 116:161, 1936.

7. Wiggers, C. J.: Defibrillation of the Ventricles, editorial, Circulation Res. 1:191, 1953.

8. Senning, A.: Ventricular Fibrillation During Hypothermia, Used as a Method to Facilitate Intracardiac Operations, Acta chir. scandinav. 109: 303, 1955.

9. Peddie, G. H.; Creech, O., Jr., and Halpert, B.: Structural Changes in the Heart Resulting from Cardiac Massage, Surgery 40:481, 1956.

10. Johnson, J., and Kirby, C. K.: Surgical Treatment of Ventricular Fibrillation, Ann. Surg. 134:672, 1951.

11. Kay, J. H.: Treatment of Cardiac Arrest: An Experimental Study, Surg. Gynec. & Obst. 93:682, 1951.

12. Lape, H. E., and Maison, G. L.: Cardiac Resuscitation and Survival: Influence of Rate of Manual Compression, Type of Countershock, and of Epinephrine, Am. J. Physiol. 172:417, 1953.

13. Leeds, S. E.: Cardiac Resuscitation, J. A. M. A. 152:1409, 1953.

14. Hooker, D. R.; Kouwenhoven, W. B., and Langworthy, O. R.: Effect of Alternating Electrical Currents on the Heart, Am. J. Physiol. 103: 444, 1933.

15. Riberi, A.; Kajikuri, H., and Shumacker, H. B., Jr.: Ventricular Fibrillation in the Hypothermic State: III. Management of Coronary Air Embolism and Ventricular Fibrillation, A. M. A. Arch. Surg. 72:502, 1956.

16. Shumway, N. E., and Lewis, F. J.: Induced Ventricular Fibrillation for Experimental Intracardiac Surgery Under Hypothermia, Ann. Surg. 143:230, 1956.

17. McMillan, I. K. R.: Cardiac Resuscitation, Brit. M. Bull. 11:229, 1955.

18. Mackay, R. S.; Mooslin, K. E., and Leeds, S. E.: Effects of Electric Currents on the Canine Heart, with Particular Reference to Ventricular Fibrillation, Ann. Surg. 134:173, 1951.

19. Wiggers, C. J.: Physiologic Basis for Cardiac Resuscitation from Ventricular Fibrillation: Method for Serial Defibrillation, Am. Heart J. 20:412, 1940.

20. Kirby, C. K.; Jensen, J. M., and Johnson, J.: Ventricular Fibrillation in Hypothermic Dogs, S. Forum (1954) 5:110, 1955.

21. Beck, C. S., and Mautz, F. R.: Control of the Heart Beat by the Surgeon, Ann. Surg. 106: 525, 1937.

22. Stover, J. H., Jr.: Electric Defibrillator for Cardiac Resuscitation, U. S. Armed Forces M. J. 2:57, 1951.

23. Wesolowski, S. A.; Gordy, E., and Cole, D.: A Simple Defibrillator Electrode, J. Thoracic Surg. 31:649, 1956.

24. Kouwenhoven, W. B., and Kay, J. H.: Simple Electrical Apparatus for the Clinical Treatment of Ventricular Fibrillation, Surgery 30:781, 1951.

25. Glenn, W. W. L., and Sewell, W. H., Jr.: Experimental Cardiac Surgery: IV. Prevention of Air Embolism in Open Heart Surgery; Repair of Interauricular Septal Defects, Surgery 34:195, 1953.

DISCUSSION

ON PAPERS BY MCCARTHY, KRAMÁR, MEYERS, DIETZ, AND WILLIAMS AND KORTZ AND SWAN

DR. DEAN SAUER, St. Louis: It would not be presumptuous, I believe, to say that the surgeon has presently climbed the very highest rungs of his technical ladder, and with his climbing he has constantly reduced surgical morbidity and mortality. By the same token, one might say that further progress will be made by a continuous study of the pathophysiology of surgical disease, as has been so beautifully exemplified by the work of Drs. McCarthy and Kortz and Swan when they turned the light of their investigations on two or three phases of this very complex surgical problem.

Dr. McCarthy has shown that it is a very simple matter quickly to determine capillary resistance by the expedient of a small suction cup and mercury manometer, and he can then determine the minimal pressure necessary to produce a petechial hemorrhage.

He has shown that capillary resistance is increased very markedly at any time that factors which produce hypoxia in anesthesia are operative and that almost immediately there appears in the circulating blood a very noxious, a very deleterious substance, vasopressin, which when present in sufficient quantities or perhaps in a sensitive patient in even very minute quantities may produce markedly increased capillary resistance, and that this substance by its action on the vessels of the myocardium may produce complete cardiac ischemia with its resultant devastating effect—an almost instant cardiac arrest.

It may not be redundant to say that at least three things are impressive in cardiac arrest. First, cardiac arrest always seems to come at the beginning of anesthesia, or it comes when the anesthesiologist is terminating his anesthesia, and a third significant thing seems to be that at autopsy almost invariably there is absolutely no evidence whatever of demonstrable cardiac disease.

The vessels of the myocardium are to all intents and purposes within normal limits.

What practical correlation can we draw from such investigations? It would seem obvious, since Dr. McCarthy has pointed out that as long as the anesthesia was smooth, as long as it was vigorously attended, nothing occurred, but when the anesthesia became somewhat stormy almost invariably we had the immediate formation of this deleterious substance, vasopressin, with its subsequent devastating and catastrophic effects.

He has shown that patients brought to the operating room poorly prepared and poorly narcotized were the most likely to fall into this category.

He has shown further that it is incumbent upon the anesthesiologist to pay particular attention to anesthesia at its beginning and end, and I might

say it would behoove all of us never to bring a patient to the operating room too quickly premedicated.

I should like to ask Dr. McCarthy if he would be kind enough to show two slides which he has shown to me which demonstrate most forcefully what can result in the production of vasopressin in so-called minor operative procedures, and I should like to pose again one question. Namely, does Dr. McCarthy feel that in the future some substance antagonistic to vasopressin may be developed and may be used as a prophylactic in the prevention of this most disastrous of all accompaniments of surgery, namely, cardiac arrests?

Dr. Willis J. Potts, Chicago: Dr. McCarthy and associates have presented an excellent paper on the physiology of this controversial subject—cardiac arrest.

The physiology of heart action is little different from the physiology of muscle action in general except for the fact that cardiac muscle contracts rhythmically and, fortunately, continuously. Work can be done by muscle only if it is fed a continuous stream of oxygen fuel, if the carbon dioxide smoke is carried away, if sufficient transportation for both is provided, and if the contracting fibers are not paralyzed with excessive drugs.

It cannot be repeated too often that the sole function of the heart is to beat. It wants to beat, and it will keep on beating so long as its metabolic processes are optimum.

In our experience with approximately 1400 operations for congenital heart disease we have had few cases of cardiac arrest—in 500 operations for patent ductus arteriosus, none. When cardiac arrest has occurred, it has been due to specific causes, such as hemorrhage, interrupted circulation, hypothermia, and uncontrollable hypoxia. In other words, the metabolism of the heart was interfered with to a degree that made it impossible for the muscle to contract.

A normal or a near-normal heart will not stop during operation so long as the anesthesiologist gets plenty of oxygen into the patient, removes the CO_2, and avoids poisoning with excessive or ill-chosen anesthetic agents. The moment-to-moment alert anesthesiologist can in routine operations eliminate the specter of cardiac arrest from the operating room.

Dr. Harry H. McCarthy, Omaha: I am sorry that the short period of time did not allow me to make one or two points that were of necessity omitted.

First of all, I should like to thank Dr. Dean Sauer for his remarks and to congratulate him on his appointment to the Executive Board.

I should also like to thank Dr. Potts. On the question of oxygen, it is obvious that it is extremely important, but there are times that it is not possible to determine clinically, or to control, sufficient oxygenation.

By means of capillary resistance determination, one can predict three or four minutes before the anesthetist can that there is something undesirable taking place. Bradycardia and the slight hypertension indicating subclinical anoxia is present and is the stimulus for the production of histamine and, in turn, the release of vasopressin. When we speak of vasopressin, we are talking about a substance that is similar to Pituitrin.

I can recall occasional cardiac arrests which occurred in situations where oxygen apparently had little or no influence in the arrest. The sudden cardiac arrest resulting from topical application of Pontocaine to the pharynx is a good example. This toxic substance, in certain cases, probably releases histamine, then vasopressin, and cardiac arrest occurs.

Another example of cardiac arrest not directly due to anoxia is the sudden death of animals in our experimental laboratory. We lost several animals while performing total sympathectomies. Cardiac arrest occurred toward the end of the procedure. We soon realized we were not giving them atropine preoperatively. Subsequent to the administration of proper medication we had no further trouble.

Anoxia may occur during simple procedures, such as tonsillectomy. Two young brothers had tonsillectomies the same morning performed by a competent surgeon. One experienced smooth induction, with no fear or excitement. The bioassay revealed no evidence of vasopressin and no chloruretic effect. The patient's brother was fearful, frightened, and excited during the induction, and assays revealed large amounts of vasopressin.

All patients with high vasopressin assays do not die. Many times it is present when we least expect it, and, if the patient is not sensitive, little untoward reaction will occur.

During tonsillectomy and other oral procedures constant suction of oxygen causes anoxia. Vasopressin is released, and death occurs. Autopsies on these patients show nothing. In earlier years it was thought that such patients died of an enlarged thymus or "status lymphaticus."

One of the residents on the obstetrical and gynecological service studied preeclamptic and eclamptic patients. Every one of his patients' blood assays showed large amounts of vasopressin. Vasopressin not only affects capillary resistance but it causes urinary findings such as hematuria, albuminuria, casts, and oliguria. Cerebral edema and convulsions may also result from patients sensitive to vasopressin.

Consider the patient with a foreign body—a fragment of glass in his hand. He is taken to the operating room. A minute amount of Pen-

tothal Sodium is administered. Within a few minutes, before an incision is made, bronchospasm and cardiac arrest occur. Bronchospasm causes anoxia and, possibly, the release of vasopressin and death.

Time does not permit further discussion. I should like to say this is not a complete study. We are still continuing it. We are studying various types of anesthesias under different circumstances, hoping for further explanation of the presence of this toxic substance.

DR. HENRY SWAN, Denver: I think it is obvious from our laboratory experience which we reported here this morning that we would genuinely urge any of you who have occasion to have to defibrillate the fibrillating ventricle in a patient to avoid the electrical damage which occurs to the myocardium because of the high myocardial-electrode interface resistance. And the use of some padding which is soaked in an electrolyte-containing solution of isotonic saline is very effective in this regard.

In addition, though, we should like to make a plea to those who are studying the mechanisms of ventricular fibrillation to report their results in terms of longer survival.

It is obvious that the first step is the restoration of a normal cardiac rhythm of some kind, and this can be done very readily by electrical shock technique in both warm and hypothermic animals, including man. But the pay-off is the long-term survival, and the continuance of the regular beat, and not a damaged myocardium which causes a subsequent acute and fatal arrhythmia. A lot of work is going on at the present time, and has been reported, with failure to mention the long-term results. I think it would be helpful to us all if we made it a practice to report these.

The Closure of Cardiac Septal Defects

The Beginning of By-Pass Surgery at a Medium-Sized Private Hospital

WILLIAM H. MYERLY, M.D.; TOM D. THROCKMORTON, M.D., and JOHN E. GUSTAFSON, M.D.,
Des Moines, Iowa

Three years ago the staff at Iowa Methodist Hospital, in Des Moines, established a laboratory for cardiac catheterization studies. As we physicians, and the technicians who assist us, acquired experience in the performance of that work, and as we processed our large backlog of diagnostic problems, we turned up a substantial number of congenital cardiac defects for which we could provide no treatment. Extracorporeal circulation at that time had only recently facilitated the performance of open cardiac surgery, and we referred a number of our most urgent cases to the University of Minnesota or to the Mayo Clinic, at Rochester, Minn., for treatment. The results of surgery in those patients were most dramatic, and suddenly there was new hope for a multitude of previously incurable cardiac invalids.

Along with our fellow specialists the world over, we took pride in the techniques that had been put to use elsewhere, but our pleasure was no more than vicarious. As far as we were personally concerned, the new successes might well have been no more than parts of a science-fiction fantasy. Quite promptly, however, we were brought to earth by the personnel of our cardiac laboratory. "How soon," they asked, "are you surgeons going to master these techniques? How quickly can you learn the surgical procedures that will complement our diagnostic studies?"

This report will outline the means by which private enterprise in a private hospital found a solution for each of the parts of a complex problem.

Read at the 64th Annual Meeting of the Western Surgical Association, Cincinnati, Dec. 1, 1956.

A Basic Knowledge of Cardiology Had to Be Acquired

It must be admitted that neither of the two of us who undertook to prepare ourselves for this work was able at the outset to distinguish a tetralogy of Fallot from a Eisenmenger complex. One of us set about to review cardiac embryology, physiology, anatomy, and pathology. He became an ubiquitous figure at autopsies; he dissected hearts, both animal and human; he became an intimate of every preserved heart in the department of pathology. In short, all of his spare time was consumed by this basic study for more than three months.

An Experimental Laboratory Had to Be Built

The Iowa Methodist Hospital has no university connections, and it had no facilities for animal experimentation. An operating room was set up in an area that previously had been used for polio outpatient care, and, through the cooperation of a local veterinarian, the preoperative preparation and postoperative kenneling of the experimental dogs were managed. At $10 each, dogs were brought into Des Moines by express, and ultimately about 150 animals were used. The Hospital furnished sterile supplies and drugs, and special instruments and equipment were secured through a grant from the Iowa State Department of Health.

A Pump Oxygenator Had to Be Constructed

A device for extracorporeal circulation, designed to permit open cardiac surgery by means of a "by-pass" technique, was built to resemble the University of Minnesota's

DeWall oxygenerator, and Lillehei and his associates there gave not only their good example but also their moral support and guidance on many occasions. Because we built our pump oxygenator in a home workshop, we are among the few surgeons in the world entitled to list the cost of a lathe and a drill press among their tax-deductible expenses for surgical equipment.

As its name implies, the pump oxygenator consists of a pumping mechanism that carries venous blood away from the body to an oxygenator, where respiratory exchange occurs, and then pumps it back into the arterial vessels of the body, thus by-passing the heart and lungs. In this mechanism the functions of the right and left sides of the heart are performed by two Sigmamotor finger pumps, in which "fingers" milk the rubber tubing, thus propelling the blood in a pulsatile manner.

The oxygenator is a vertical plastic tube through which blood is pumped and oxygen is bubbled. The actual respiratory exchange occurs in this column of foaming blood. The blood is "defoamed" in a horizontal plastic tubular chamber coated with Silicone. The bubbles burst, releasing the excess oxygen and carbon dioxide through a vent. The liquid, oxygenated blood then flows down through a helix of plastic tubing, through a water bath that is necessary for temperature control, and then is pumped back into the body of the patient.

While we were developing our pump oxygenator, we found it necessary to start all over again twice. Thus, in the process we developed three complete units.

Hemolysis was initially regarded as a drawback of this type of extracorporeal circulation. But our early experimental work failed to bear out this one of our misgivings; and when we had made certain modifications in the equipment, we not only conserved blood and reduced trauma but had no more than insignificant amounts of hemolysis, even after long runs of the pump oxygenator. These determinations have been made frequently on blood both from the extracorporeal circulation and from the patient at the conclusion of the experiment or operation.

In modifying and testing our apparatus and perfecting our technique in using it, we operated upon 55 dogs.

A Sound Operative Technique Had to Be Established

As the extracorporeal oxygenator became totally dependable, we came to recognize that all of the potentialities for failure lay in human fallibility. At one time or another, as we practiced on animals, we made nearly every possible mistake and at least recognized the imminence of each of the others. We devised a step-by-step routine for placing a dog "on the pump" and worked out a "check-off" system as a means of avoiding human frailty.

There are no essential differences between our technique and that of Lillehei. The patient is weighed, and connections are made for electrocardiogram and cardiophone leads. Two electrical heating pads are placed on the operating table, one above and one below the buttocks of the patient. The plate from the electrosurgical unit is placed beneath the buttocks. If the heating pad and the plate are in contact, a third-degree burn will almost certainly result. The patient is anesthetized with intravenous thiopental (Pentothal) sodium, enough gallamine (Flexedil) triethiodide (tri[diethylaminoethoxy] benzene triethyliodide) being used to allow intratracheal intubation for positive-pressure respiration. A cutdown is made over the saphenous vein in the groin, and a polyethylene (Polythene) catheter is passed through the femoral vein and into the vena cava for the purpose of fluid and blood replacement, anesthesia, and the withdrawal of blood for laboratory determinations. A constant-recording thermometer is inserted in the rectum.

When the patient has been placed in the supine position and has been draped, a transverse transsternal incision is made in the fourth interspace. All bleeding points

are controlled by electrocoagulation, except for the internal mammary vessels, which are controlled by suture ligatures. The pericardium is opened wide, and it is especially important that bleeding from all pericardial vessels be controlled. After the patient has been heparinized, bleeding from even these tiny vessels may be disastrous.

The heart is examined, especially as regards chamber hypertrophy, location of thrills, and location and size of major vessels. The extent and nature of defects having been determined, if possible, the inferior and superior venae cavae are encircled by tapes. The first portion of the aorta is then encircled by another tape, to be held in a Rummel tourniquet. This arrangement permits temporary constriction of the coronary blood flow and allows manipulation in a dry field for periods as long as 30 seconds.

At this point we heparinize the patient, using a quantity of heparin that will amount to 1.5 to 2.0 mg. per 100 cc. of the entire calculated blood volume of both pump oxygenator and patient.

The left subclavian artery is then encircled and ligated as distally as possible. Proximally, a Potts clamp is then placed across the vessel; the wall is incised between the clamp and the suture, and a plastic catheter is fed into the aorta and is held there by means of several ligatures. (On several occasions when a right-sided aortic arch has been noted, the arterial cannula has been introduced through the femoral artery.) This catheter is connected to the outflow of the extracorporeal circulation.

The right auricular appendage is then held while two purse-string sutures are taken in its wall and two incisions are made. Plastic catheters are directed through these incisions into the superior and inferior venae cavae. (When a left-sided superior vena cava has been found, it has been cannulated through the coronary sinus.) These catheters are joined by a Y-connecting-tube to the inflow of the pump oxygenator. When the previously placed caval tapes are tightened about these catheters, the entire venous return of the body may be shunted away from the heart and into the extracorporeal circulation.

A specially constructed nonobstructing plastic suction tip is then connected to the third Sigmamotor pump so as to provide for the return of the coronary sinus flow into the oxygenator. A separate and clearly marked suction tip is connected, through a 5000 cc. graduated flask, to a high-speed suction, so as to allow rapid clearing of the field if abnormal bleeding is encountered and to permit moment-to-moment measurement of blood loss in order that simultaneous replacement may be carried on.

The oxygen supply to the oxygenator is turned on; the pumps are started; the caval tapes are tightened, and the inflow and outflow of the system are carefully balanced. We have attempted to circulate 40 cc. of blood per kilogram of body weight per minute. Actually, the flow has varied from 35 to 60 cc., and the average for the cases herewith presented was 45 cc. per kilogram per minute. We are gradually raising the flow rate, for patients seem to "do better" with a high arterial flow.

As the pump oxygenator begins work, the heart becomes flaccid, and its beat is slowed. Stay sutures are placed in the wall of the right ventricle, and an incision is made in it paralleling the left anterior descending branch of the left coronary artery. A definite attempt is made to place this incision in an area where branches from this vessel interdigitate with the right coronary artery, for by that means the likelihood of an area of myocardial ischemia can be reduced. As this incision is made, several tiny arteries spurt briskly—a phenomenon which always impresses the observer with the efficiency of the mechanical extracorporeal circulation. Actually, any major bleeding points are controlled by Babcock clamps, which serve also as tractors for exposure within the right ventricle. At this point, the low-speed suction tip is put into the right

ventricle, and the sheet of blood from the coronary-sinus return is carried out of the field and back to the oxygenator.

Most ventricular septal defects can readily be seen, and if the aortic valve is at all incompetent, oxygenated blood will well up through the defect. This latter flow of blood may be stopped at will by the exertion of a temporary pressure through the Rummel tourniquet upon the aorta. Not uncommonly, the flow through the septal defect may seem to come from multiple openings, as it wells up through the cordage of the tricuspid valve and the papillary muscles. These latter structures may be divided at the ventricular wall and held aside by stay sutures so as to provide the necessary exposure.

A finger passed up toward the pulmonary valve may reveal an infundibular or a valvular stenosis. The former condition can also be visualized promptly, thus making subsequent excision possible. A finger slipped through the tricuspid valve can explore for atrial septal defects. Also, as one looks through a ventricular septal defect, the cusps of the aortic valve can be seen bulging downward—sometimes too close for the investigator's complete comfort.

The simple ventricular septal defect has been easily closed by means of a few nonabsorbable surgical (silk) sutures taken in its edges. Those at opposite ends of the defect are routinely passed through a strip of polyvinyl formalinized (Ivalon) sponge, and those in the middle of the defect are tied over the sponge, which serves not so much as a patch as, rather, an effective caulking material. A small multifenestrated plastic catheter is introduced into the left ventricle through the ventricular septal defect, and 50 cc. of saline is injected as the last of the sutures are tied and as the catheter is withdrawn. It is thought that this maneuver may flush air from the ventricle and prevent air embolism from this source.

If an infundibulbar type of pulmonary stenosis is present, it is then resected. We use a tonsil punch equipped with a basket to hold the fragments. If the rarer valvular stenosis is present, a valvulotomy is done, and dilatation is completed by means of Hegar dilators.

Should the lesion be an atrial septal defect, the primary cardiotomy is done in the right atrium, and the defect is quickly closed, under direct vision, with a continuous silk suture. There is none of the necessity for haste that is associated with other techniques. When the cardiac lesion has been corrected, the cardiotomy incision is quickly closed with a continuous silk suture. The tapes are then taken from the venae cavae, the superior one first, and the total volume of blood is balanced between the patient and the pump oxygenator. One watches the patient's heart "take over" after the mechanism has been shut off.

When it is certain that all is well and that it will be unnecessary to return the patient to the pump, the cannula in the subclavian artery is removed, and the vessel suture is ligated proximally and then divided between the ligatures. Similarly, the two caval cannulae are withdrawn, and the wounds in the auricular appendage or atrium are closed by suture or ligature, as seems most feasible. At this point, an arbitrary dose of protamine sulfate is injected slowly into the patient, the amount being approximately 1.5 mg. for each milligram of heparin previously used. This is somewhat greater than the amount theoretically required to counteract the circulating heparin.

Throughout all stages of this procedure, except during actual cardiotomy, the viscera are moistened, and a clear field is maintained by flushing with a 2 mg. per 100 cc. solution of heparin in isotonic saline.

When it has been determined that the field and the wound are dry, the pericardium is partially and loosely closed by means of a few sutures of silk. Multifenestrated plastic catheter drains are let into each side of the chest through anterolateral stab wounds and are located in the posterior thorax, extend-

ing to the apex on either side. These are for the purpose of closed-suction drainage. The sternum is stabilized by wire sutures, and the thoracotomy is closed. On several occasions a resection of portions of the transected sternum has aided in the closure of the chest.

The establishment of a rapid, simplified technique is important, but the greatest necessity is the formation of an operating team, the personnel of which can be unchanging. The members must seek perfection. The pride of accomplishment must be a pride of team effort and cooperation. Frequent substitution "from the bench" or the inclination of one of the members to be a prima donna can stifle such a spirit.

A Trial Run Had to Be Made Under Actual Operating-Room Conditions

Once the personnel of our team had been established and the by-pass techniques had become routinized, the entire operation had to be transplanted to the operating suite of the Hospital. Two days before we first used the extracorporeal circulation upon a patient, the entire personnel and equipment were transplanted to the operating room, where a "shake-down cruise" was conducted, the subject being a large dog. This dress rehearsal was of inestimable value, for it pointed up certain mechanical and geographic difficulties that had not previously been apparent. For example, it was found that the only emergency electric circuit served the actual operating lights, and a special outlet had to be installed to serve our pumps. We had other extraordinary electrical requirements, and a total of nine separate outlets had to be provided before our set-up was complete. A special power cable brought from an adjoining room supplied some of them. All electrical outlets are of the "lock-in" type, and all cables are held to the floor by a sheath of adhesive tape. The most desirable location for all of the required auxiliary equipment can be determined only by trial and error.

Community Interest Had to Be Fostered

Actually, there were two communities to which the project had to be sold: (1) the tightly knit medical-hospital staff community and (2) the nonmedical lay community.

It was essential for the surgical personnel to take the medical community into its confidence, because added work and responsibilities are more lightly shouldered if they are recompensed in gratitude and understanding. The Hospital's administrative staff had to be convinced of the importance of the project and of its probable value to the medical care of the area served. The operating-room personnel had to learn new techniques, new instruments, and a whole new operating-room set-up. The laboratory and its forces had to be marshaled. The blood bank was likely to be overwhelmed by the requirements of cardiac surgery of this type unless a definite plan of action were formulated. The clinical chemist had to ready a group of unusual procedures for rapid and accurate determinations. In other words, it was necessary that the pathologist be made a confirmed and ardent advocate of the project. The radiologist had to expect to be called upon at any moment for what might seem to be arbitrary and unnecessary determinations. The services and support of an expert bronchoscopist were essential. Most vital of all, the entire professional staff of the Hospital had to be brought to the realization that the project was not merely a grandiose experiment. They needed assurance that every precaution was being taken in the interest of the patients. The physicians had to know that every safeguard, human and mechanical, had been provided. It was necessary that the discipline of the project should be so thorough that it could provoke only favorable regard.

The nonmedical community contained many persons who were important to the project. The advice and counsel of a veterinarian were required. The help of expert machinists was essential to the manufacture of certain elements of the extracorporeal

oxygenator. Of more general importance was the approval of public-spirited citizens of the community. They had to be alerted to the project, kept abreast of its progress, and conditioned not to expect a favorable outcome in each patient on whom the new procedures were performed.

A Postoperative Routine Had to Be Established

The case of a patient in whom a septal defect has been closed by means of the by-pass technique varies from any other thoracotomy only in two respects.

Respiratory difficulties are multiplied by the bilateral transsternal thoracotomy that is used. A good airway is more difficult to maintain, and the patient is encouraged to practice coughing preoperatively, if possible, and also postoperatively. Routine interval roentgenograms are taken of the chest, and bronchoscopy is done on minimal indications. Tracheotomy is done if multiple bronchoscopy is required. A clean tracheobronchial tree can be more readily maintained if direct and frequent aspiration is provided.

Hemorrhage is the danger that deserves most comment. Hemorrhage is a complication to be anticipated following any surgical procedure, but the overwhelming hemorrhage that can occur after an operation that includes the use of a pump oxygenator is, to say the least, different! The crux of the matter is that the surgery has been performed upon a heparinized patient, and on one possessed of a defect, such as the tetralogy of Fallot, that is known to contribute to a hemorrhagic tendency. In addition, the patient's blood has been mechanically traumatized by being passed through an extracorporeal circulatory system. Without invading the domain of the hematologist, one can say that the exact interrelation of heparin and protamine is not known, but it is neither certain nor quantitative. The roles of the pump oxygenator and the syndrome of the tetralogy of Fallot are even less completely understood, but nonetheless it is certain that they have a tendency to produce a hemorrhagic status.

Hemorrhage of this type is not common. If it occurs, it tends to follow an uneventful operation, and it presents during an otherwise satisfactory postoperative course. Suddenly both thoracotomy tubes begin to spout blood in amounts of 200 to 500 cc., each within a few minutes. The amount increases to the point where it is difficult to supply blood at the rate that it is being lost. One envisions the bleeding of a major vessel or an incompetent suture line in the myocardium. Repeat and urgent thoracotomy has been done on two occasions, but no major bleeding point has been found accountable. All traumatized surfaces inexorably weep blood, and the blood does not clot. In the first instance, this condition responded to empirical treatment with intravenous fibrinogen. Subsequent studies have proved the presence of fibrinolysins, and routine determinations have been established, by means of which this hemorrhagic tendency can be forecast in time for treatment of the tendency rather than of the actual condition.

Our laboratory has entitled this determination "semiquantitative clot retraction time," and we feel that an account of it will prove valuable.

1. Five cubic centimeters of whole blood is put into a graduated centrifuge tube.
2. This is incubated in a water bath at 37 C for one hour.
3. The total quantity of blood and serum is read from the graduations.
4. The clot is removed by means of a wire hook.
5. The remaining serum and cells are centrifuged.
6. The quantity of serum expressed is measured.
7. A hematocrit is done on whole oxalated blood.
8. The serum present in the specimen is calculated.

Example: 5 cc. whole clotted blood hematocrit 42%; plasma 58% $5 \times 0.58 = 2.90$ cc. serum

9. Divide the serum expressed in clotting by the volume of potential serum obtained as above.

Example: 2 cc. expressed from 5 cc. of clot

$$\frac{2}{2.9}=68.9\%$$

10. Results are expressed as a percentage of potential residual serum. Values considered normal are in the range of 70%-75%. If the value is lower than 60%, we feel that it indicates a diminution of circulating fibrinogen and an impending hemorrhagic state. To such a patient, we give 1 gm. or more of fibrinogen, depending upon his weight.

Indications for Surgery on Cardiac Septal Defects

There are four indications for surgery on cardiac septal defects: (1) elevated pressure in the right ventricle; (2) elevated pressure in the pulmonary artery, unless pulmonary stenosis is suspected; (3) enlargement of the heart disclosed by x-ray examination, and (4) a large left-to-right shunt.

Experience with the Closure of Septal Defects

We closed our first ventricular septal defect on Feb. 22, 1956, and the patient is alive and well today. Other surgical centers have had far greater experience than ours, but, inasmuch as our circumstances are somewhat different, perhaps our experience may be of interest.

To date, we have had 17 patients on the pump oxygenator. This discussion is limited to the 13 of them who had septal defects. The other four had (1) incorrectly diagnosed patent ductus, (2) truncus arteriosus, (3) common ventricle, and (4) coarctation of the pulmonary artery. Of the cases covered by this report, five had pure ventricular septal defects; five had tetralogy of Fallot, i. e., ventricular septal defect and pulmonary stenosis, and one had a ventricular septal defect complicated by a hugely hypertrophied ridge of muscle that crossed the right ventricle and, for practical purposes, divided it into two chambers. Two had atrial septal defects.

The length of the operation varied little—from 1 hour and 50 minutes to 2 hours and 45 minutes. The two longest operations were performed upon patients who had undergone previous attempts at cardiac surgery elsewhere. In each case the pericardium had been opened, and the lesion had been found irremediable by the closed technique that the surgeons were prepared to employ. The average duration of our operations has been 2 hours and 20 minutes.

The period during which our patient has been "on the pump"—i. e., the duration of extracorporeal circulation—has varied from 8 to 29 minutes, the average having been 20 minutes. We have noted that approximately three minutes is required for balancing of inflow and outflow of the system before cardiotomy is done.

Blood electrolyte studies done in the immediate postoperative period have all been within normal limits. The blood pH studies have been in the lower range of normal.

Hemolysis of blood has varied but has never been a serious factor in our by-pass technique. The average amount of hemolysis in the blood remaining in the pump oxygenator after surgery has been 52 mg. per 100 cc. Any amount less than 200 mg. per 100 cc. has been considered safe.

The average hospital bill for these patients was $1,091, the extremes being $871 and $2,201.

Results

Five ventricular septal defects have been closed, and all of the patients have clinically recovered.

One patient who had a ventricular septal defect with a hypertrophied muscular ridge is unimproved. Fifteen grams of cardiac muscle was resected before the defect could be visualized. The patient has been in right heart failure for three months, but we hope that in time the weakened muscle will compensate.

In five patients we closed ventricular septal defects and resected infundibular pulmonary stenoses. Four of these patients are living and clinically cured. One died suddenly 40 hours following an uneventful operation. She was thought to be blind 24

hours after surgery, and she died after 8 hours of convulsions. An autopsy failed to show a cause of death. The heart repair was excellent.

Two patients in whom atrial septal defects were closed have recovered clinically.

Comment

Our experiences in building, perfecting, and using a pump oxygenator in open cardiac surgery are proof that these techniques are practical, are worth while, and need not be confined to what are known, in the vernacular, as "medical centers."

Our experiences also point up a great and widely credited fallacy in this field of "bypass surgery," a fallacy that is keeping this technique from multitudes of patients who need help today. Too many surgeons mistakenly believe that certain types of machines, or modifications of machines, are essential to success in this type of work. On the contrary, we believe that there are at least half a dozen different mechanical devices that will satisfactorily pump oxygenated blood into a patient. Any one of them can be made mechanically dependable.

The skill and cooperation of the medical and surgical team—not the choice of machine—determine the success or failure of the technique. A rigid discipline must be developed which rediscovers and enshrines the required basic principles. When the dependability of the human factor approaches that of whichever pump oxygenator is used, then—and then only—should a series of operations be commenced.

There are some other facts which we have discovered or rediscovered, and which we deem important.

Infundibular Stenosis.—Several times we have cut across a large coronary artery during the resection of an infundibular stenosis. The bleeding from this source is vigorous, but it would seem to be of little concern, since it is into the right ventricle, and hence back into the vascular system. We believe that such a vessel should be ligated. The blood from this source is under aortic pressure, and the bleeding, occurring as it does into a chamber of lower pressure, may well draw away some of the blood that should be delivered to the myocardium. It is possible that a relative ischemia of the myocardium could result.

Variability of Ventricular Septal Defects. The difference between a simple ventricular septal defect and one associated with a pulmonary stenosis is striking. The former has a white, tough, fibrous margin. This thin, strong edge can be sutured easily and dependably. A ventricular septal defect with a tetralogy of Fallot, on the contrary, usually has a thick, muscular margin which can be sutured less dependably and which multiplies the surgeon's opportunities for interfering with the cardiac conduction system and causing a heart block.

Air Embolism.—Though we lack proof, we believe that the single death in our series was the result of air embolism. It is probable that air, trapped in the left ventricle, eventuated as cerebral emboli. In subsequent operations in our series, we have passed a small, multifenestrated catheter through the defect and into the left ventricle. Through this we have injected 50 cc. of saline solution just as we closed the defect by tying the sutures. The greater efficacy of multiple jets of saline in flushing air from the ventricle will be apparent if one visualizes them and the old-fashioned "whirling-spray" douche tip.

In our animal operations, we have flooded the operating field with carbon dioxide on several occasions. Since this gas has twice the density and 60 times the solubility of nitrogen, it readily displaces air. We have injected 10 cc. of carbon dioxide rapidly into the carotid arteries of the dogs without incurring any ill effect, either immediate or delayed. The use of a carbon dioxide atmosphere may become a feasible surgical technique as surgery of the left ventricle is developed.

Cardiac Arrest.—Several hours following surgery, one patient in whom we had repaired a tetralogy of Fallot had cardiac

arrest for 45 minutes. Rhythm was successfully reestablished. Cardiac massage and controlled-pressure respiration were carried out. Blood was rapidly infused through a cannula in the inferior vena cava. We believe that this infusion accounted for the rapid diastolic filling of the heart, and the increased mechanical advantage of massaging a full heart probably explains the successful outcome in that case. The patient is now keeping up with his class in school. Raising the venous pressure so as, in turn, to increase the arterial pressure during massage is a simple expedient, and the excess of blood can subsequently be removed if the resuscitated heart becomes embarrassed.

Intrapericaraial Exploration.—The surgeon should not attempt this procedure unless he is willing and ready to undertake a repair that may require a by-pass technique. The two patients upon whom we reoperated demonstrated that fact to our entire satisfaction. Those two children had been "explored" elsewhere, in the hope that they might be aided by some sort of "closed technique." The extensive pleural adhesions made reoperation difficult, but far more vital was the complete obliteration of the pericardial cavity. The entire heart, in each case, was ensheathed in white, tough fibrous tissue that completely concealed the location of the coronary vessels and made the caval dissection extremely hazardous. This fibrous envelope was entirely avascular, and for that reason we were dubious as regards any chances of supplementing the coronary flow by stimulating the vascular adhesions.

Both the patients have progressed satisfactorily since their operations, but in each case the previous, and wholly ineffectual, opening of the pericardium had been responsible for greatly increasing both the risk and the length of our surgery.

Summary

A pump oxygenator of the DeWall type has been built and found totally dependable.

A surgical team, using this pump oxygenator, developed the discipline and techniques necessary to take open cardiac surgery into the operating room of a private hospital.

The team has repaired 13 cardiac septal defects by this method. Eleven patients are clinically cured; one is unimproved, and one is dead.

Factors considered of interest and of importance are discussed.

Equitable Building (Dr. Throckmorton).

DISCUSSION

DR. ROBERT TIDRICK, Iowa City: Dr. Myerly and his associate, Dr. Throckmorton, were unjustifiably modest in the quantitative run-down of the various contributions to this procedure. Actually, the development of Dr. Myerly's basement machine shop and the effort that he and Dr. Throckmorton have put into this project, in terms of their own time and money, have been quite considerable.

Now, this work has, I think, a good lesson for the rest of us, and that is that one does not need an extensive research institute in order to make significant contributions to this intriguing field of surgery.

The workmanship that Dr. Myerly has put into this project has been most interesting for those of us who are neighbors and who have had an opportunity to see his equipment. The results that he demonstrated here, 12 out of 13 patients living, bespeak the skill and patience and the real courage he has put in.

DR. WILLIS J. POTTS, Chicago: The most important feature of this presentation is the fact that this work was done in a hospital not connected with a university, with all its research facilities. It is a stimulating and inspiring story of what can be done if the fire of enthusiasm and the will to succeed burn with a consuming flame. What has been accomplished by these men in a private hospital is commendable enough. What is of far more interest is the fact that the experimental work was done in a makeshift laboratory constructed in an abandoned building. Not everyone in the practice of surgery can be associated with a heavily endowed university and have at one's call animals, caretakers, fellows in cardiology, technicians, chemists, physiologists, and engineers. It seems appropriate to underscore an old adage—it's not the building but the man that counts.

Intracardiac surgery is new and spectacular. The thrills of success are still clouded by the agonies of failure. How far will intracardiac surgery go? Which oxygenator will prove most effective? What will late results be? Will patches remain in place? Will scars in the ven-

tricle lead to aneurysm formation? These are a few of the questions which the future must answer.

I have had considerable laboratory and some clinical experience with intracardiac surgery, but of that I do not wish to speak today. Rather, I want to present a challenging problem for some other ambitious and imaginative young man to study. Let's not allow intracardiac surgery to run away with itself. Here is a problem crying for a clearer answer. Which interventricular septal defect should be closed surgically? We have accumulated in our files at the Children's Memorial Hospital during the past 10 years the histories of 1000 children with a clinical diagnosis of interventricular septal defect. Certainly, not all of them need operation. We have in our rather extensive pathological collection of congenital hearts only one in which death was due to an isolated interventricular septal defect. This fact may be of no significance, but does suggest caution in selecting patients for operation.

Questions suggest themselves. What is the life history of patients with isolated interventricular septal defects? When and why does pulmonary hypertension occur? Should operation precede the beginnings of pulmonary hypertension? How long can one live comfortably with a 5 cm., 1 cm., 1.5 cm. hole in the interventricular wall?

We need a better method of determining which patient should be subjected to intracardiac closure of his interventricular septal defect. To other energetic workers I say, "Go find an abandoned building and bring us the answer."

Dr. R. Morton Bolman II, Fort Wayne, Ind.: I want to congratulate Drs. Throckmorton and Myerly on their outstanding accomplishment. I could not resist the desire to say a word, because we have been undertaking the same sort of problem in Fort Wayne, Ind.

My partner, Dr. Robert P. Lloyd, was in his chief year as resident in general surgery in 1949, and, though he was very anxious to get back with his family, I prevailed on him to stay another year in a cardiovascular center with Charlie Bailey. During that year I stayed at home and got geared up with the things he kept writing me and telling me we would need. When he came back, I went away several times and, on one of these trips, I took two of the internists from our area with me. We sent three nurses to the center for a month apiece and sent our recovery-room nurse for two weeks. In July, 1950, the middle of July, we undertook our first cardiovascular procedure.

Dr. Throckmorton and Dr. Myerly are far ahead of us, for we have not yet undertaken anything that involves hypothermia or shunts; but in the three and a half years since July, 1950, we have procured a Fairchild camera, a pressure transducer, all the equipment for angiocardiography, a Van Slyke apparatus, and all the instruments and things necessary to go along with it. As Dr. Potts has pointed out, this necessarily in a situation like ours has to be at our expense.

We are very proud that at the end of three years we are recognized by the Vocational Rehabilitation Association, the American Heart Association, and the Crippled Children's Association of Indiana, which used to be units served only by the university. Six months ago we were given the northern half of the State of Indiana to serve. Certainly, these things can be done. It is not a financially profitable undertaking. However, it provides a large group of timid people with an opportunity to get those things at home that some of them will not journey any great distance to get.

Dr. Tom D. Throckmorton, Des Moines, Iowa: First, I want to say that Dr. Myerly and I are very grateful for the discussion that has been accorded our paper. In many ways, we come from a small town; perhaps it is just an exaggerated county seat. Especially are we grateful for Dr. Potts' contribution. He is so well known in this field of cardiac surgery that when we asked one of our nurses for a Potts clamp she was inclined to reply, "Which kind?"

Our motive in making this report has been to emphasize the point that surgery of this kind can be done in an atmosphere perhaps less rarefied than that surrounding a large surgical center. We did not have a great quantity of money, and on occasions our equipment left something to be desired. Nevertheless, we did have something that is not always present in a university project—we had a million friends. Every doctor in Des Moines was behind our project, pushing and helping. Each and everyone was hoping that this project would go well, and it is our thought that help of this kind is worth more than any amount of money.

As far as I am concerned, this is a new kind of surgery. This is "team surgery," and it is the first time that surgery of this type has been carried out in our city. I suspect that many future advances in surgery will be made by this route. Until now there has always been a surgeon, an assistant, and someone at the head of the table trying to keep the patient asleep. In our present cardiac surgery set-up there is a real team. The anesthetist is considered as important as the operator. There are two surgeons at the table. The pediatric-medical service is an important facet of the after-care in the recovery room.

Actually, I am too old for this kind of surgery, although I am only 43. It is impossible for me to stay up all night and into the next day, as Dr.

Myerly and the pediatric cardiologist are often required to do. This is the work of young men.

This type of work has come to me as a real thrill. Actually my contribution has been small. I have, by and large, stayed home and taken care of the "store" while other people have done the real basic work.

I did want to bring this aspect of the problem to the attention of the Association, with the hope that what we have been able to do in a small way in our home town may be repeated many times throughout the country. Many people need this type of help, but it is only through undertaking a discipline of the type herein reported that help can be given.

DR. WILLIAM H. MYERLY, Des Moines, Iowa: It was quite a thrill to me even to lay eyes on Dr. Potts, because over the years I have seen his name and heard of him but have never had the privilege of shaking his hand.

I thought his question was this: Which of these defects should be closed? Frankly, Dr. Potts, that is a great problem in our minds also.

We have a backlog of approximately 50 patients on whom we are not presently considering operation, because we do not believe they require it at this time. In fact, I am certain that they do not need it now. We think that perhaps during the next several years new techniques will be involved and other safeguards employed which may make the operation much more satisfactory than it is even today. We do not wish to subject these patients to an unreasonable risk today. They can go on for the next two or three years in reasonably good shape, with anticipation of a more satisfactorily perfected technique should surgery be required.

We have performed all manner of mental gymnastics on this question.

I might say, briefly, that all is not gold that glitters in this type of surgery. I recall one boy who had a cyanotic tetralogy of Fallot. His oxygen saturation was in the neighborhood of 65%. He was 12 years old and had severe asthma. The first time I saw him I did not know he was going to be a patient of mine, and I thought he was dying. He was as black as the ace of spades during the asthmatic attack. He is one of the patients that gave us fits with postoperative hemorrhage. We had to open up his chest twice in the same evening, and on one occasion massaged his heart for 40 minutes. In an 18-hour period we pumped 32 bottles of blood into him. However, he is alive and well today.

The Correction of Aortic Insufficiency with a Spring Valve Prosthesis

Preliminary Report

JAMES H. WIBLE, M.D.; LYLE F. JACOBSON, M.D.; PRESCOTT JORDAN Jr., M.D., and CHARLES G. JOHNSTON, M.D., Detroit

The control of aortic insufficiency has been sought for many years. The clinical trial of the distally placed Hufnagel valve has met with some degree of success.[1] However, a method of control at the site of the leak has been sought in order to improve coronary perfusion as well as the one-third of the circulation not controlled with a distally placed prosthesis.

Many methods of proximal control, too numerous to enumerate here, have been tried, but none have met with general success.

The incompetent valve of aortic insufficiency, except for the traumatically ruptured cusp, is thickened, fibrotic, and some times calcified. The leaflets may move freely, or there may be some restriction of motion. The site of the leak, although often eccentric, seldom occurs at the periphery.

In the laboratory, after having been encouraged by the valvulogenic properties of the nylon-covered spring valve placed in the mitral area, the thought occurred to us that a similar type of prosthesis might be useful at the aortic annulus.[2]

The prosthetic frame, at first Y-shaped, then circular, was made of a metal alloy, Elgiloy,* covered with nylon. The following method is used in fabricating the prosthesis. Annealed 0.016 in. round Elgiloy wire is formed into a paddle-shape of arbitrary size that seems reasonable for the proximal aorta of dogs. The wire is then squeezed, cold, in a 35-ton press, which flattens the wire and introduces work into the material. The resulting frame is approximately 0.030 in. wide and 0.0063 in. thick. The alloy is then heated at 900 F for five hours and allowed to cool to room temperature. By introducing work into the material, and then rearranging the molecules by heat-treating, this particular combination of elements is made to acquire long-lasting spring properties. As noted in Figure 1, the distalmost part of the frame is not flattened and therefore is still malleable, even though it has been heat-treated. At this point, the frames are found to be covered with an oxidized coating which is easily removed by boiling for a short time in a solution of 4% hydrofluoric acid and 12% nitric acid.* A fairly close weave of nylon cloth is then secured to the frame with over-and-over nonabsorbable surgical (silk) suture.

Method

The Y-type prostheses were first used, and they were inserted through a trocar introduced just above the bulge of the sinus of Valsalva. It seemed that the round prosthesis would probably be preferable, and the following technique for insertion has been evolved.

Large dogs of approximately 20 kg. are anesthetized with intravenous pentobarbital, and mechanical respiration is established via an endotracheal tube. The right chest is entered through the fourth right interspace and the pericardial sac is instilled with 5 cc. of 2% butacaine sulfate. An umbilical tape is placed loosely about the superior and inferior vena cava extrapericardially above the

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From the Department of Surgery, Wayne State University College of Medicine, The Detroit Receiving Hospital, and the Dearborn Veterans Administration Hospital.

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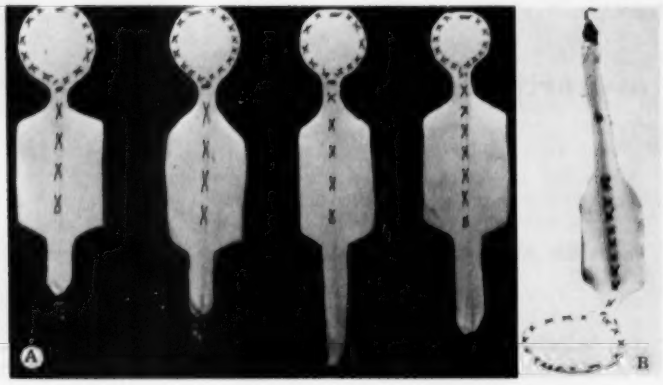


Fig. 1.—*A*, covered Elgiloy frames made in graded sizes. *B*, prosthesis with a bend made for the intra-aortic paddle. The distal handle is malleable, and a hook is made for attachment to the introducer.

level of the azygos vein on the superior vena cava. The pericardium is then incised longitudinally to its reflection over the aorta superiorly and is sutured loosely to the chest wall. Next, the right atrial appendage is turned back from the root of the aorta, and it also is sutured loosely to the chest wall. The periaortic fat pad is excised, and the right atrium is carefully dissected away from the root of the aorta, exposing the origin of the right coronary artery. A site to the right of the right coronary artery just above the thin-walled sinus of Valsalva is selected, and a small horizontal mattress suture is placed in the wall of the aorta with 00 silk or, preferably, 00 braided nylon suture.† A portion of the ascending aorta is grasped with a large Beck clamp and is incised. A polyvinyl sponge (Ivalon) sleeve with a side-arm is then sutured to the aorta (Fig. 2). The appropriate size of prosthesis is estimated and chosen; the length of the intra-aortic paddle-arm is determined, and the proper bend in the arm is made at this time. The tapes about the venae cavae are tightened, and after about six to eight beats only the blood returning through the azygos vein[4] is being pumped and the head of pressure in the aorta drops. A malleable introducer is passed through the aortic wall, inside the mattress suture, and led out through the side-arm. The prosthesis is attached and drawn retrograde into position, and the mattress suture tied down. The aortotomy is clamped, the caval tapes are released, and full circulation is restored. Once the aortic valve is explored, the time of caval occlusion for the insertion should not take more than one to two minutes. The aortotomy site is closed at leisure, and the arm of the prosthesis is sutured to the aorta (Fig. 4).

† Supplied by Ethicon, Inc., Somerville, N. J. (No. X-6128).

Results

Prostheses have been placed in the aortic area of 48 dogs, with the longest survival being 20 months. The fate of the prosthesis has been closely followed. In a few minutes the interstices of the nylon become filled

Fig. 2.—Polyvinyl sponge sleeve and metal form.

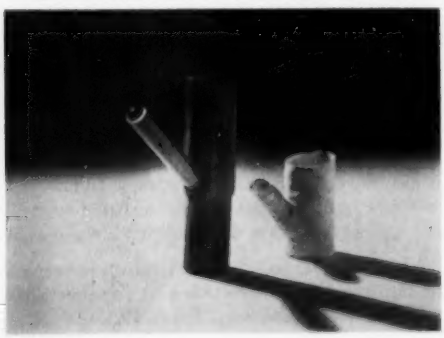
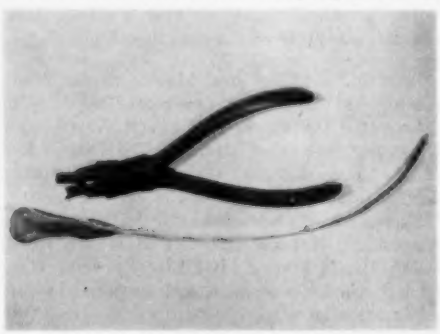


Fig. 3.—Malleable introducer, below, and shaping tool used to make the bend in the spring (see text).



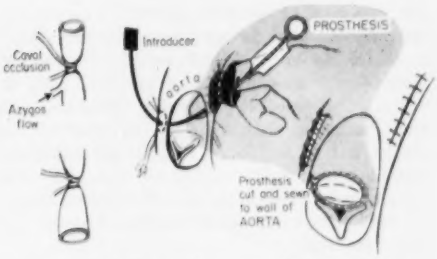


Fig. 4.—Technique of retrograde introduction.

with fibrin. Endothelial-like tissue grows out onto the prosthesis and reaches the end in 8-14 days, depending upon the size of the flap. Microscopically it is noted that the nylon is covered with fibrous tissue in which the cells are more closely packed at the surface (Fig. 5). The frame of the prosthesis can be seen fluoroscopically, and at 20 months the flap is noted to continue motion.

To date we have been unable to create aortic insufficiency that is anatomically comparable to that occurring in humans and therefore cannot demonstrate objectively its effect upon insufficiency. However, it is easily demonstrated that there is no obstruction to the outflow tract.

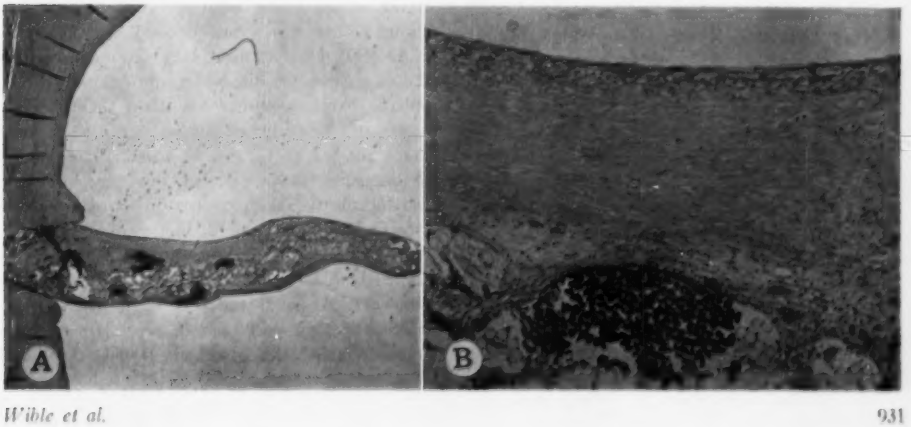
In animals with aortic prostheses killed up to 16 months, there have been no clots on the prosthesis, the host valve, or the adjacent aorta. There is smooth and firm union at the junction of the prosthesis and the aorta. The clotting mechanisms as determined by the Lee-White method have remained normal in these animals, both acutely and upon long-term follow-up. There have been no signs of emboli in the living animals.

Comment

This prosthesis fills previously formulated criteria[3] for prosthetic valvular devices in that it (1) moves and continues motion, (2) is easily inserted, (3) acquires living host tissue, (4) does not alter clotting mechanisms, (5) is tolerated within the circulation, (6) forms no clots to embolize.

The animals tolerate the short period of azygos flow very well, and the lowered aortic pressure markedly lessens the blood loss incurred while the prosthesis is being drawn through the sleeve. The flat stock used for the frame of the prosthesis gives directional motion even though it is anchored at only one point. Unipoint fixation not only minimizes unnatural eddys which could beget fibrin deposits but also simplifies insertion. In addition, the internal resistance of the spring gives shape to the flap and also prevents the valve from becoming stuck to the wall of the aorta. The thickened leaflets occasioned by disease form a good seat upon which the prosthesis can close. The valve is placed in such a manner that

Fig. 5.—*A*, low-power view of aortic prosthesis after 10 months, showing the junction with the aorta; ×5. *B*, high-power view of the above 10-month prosthesis, showing the nylon, silk, and host tissue which has invaded the prosthesis; ×90.



there is no interference with coronary flow, and coronary perfusion pressure should be improved by the increased diastolic pressure.

In the laboratory, we are working upon the problem of resecting the stenotic aortic valve and covering the free insufficiency with a spring valve. Gorlin et al.[5] have demonstrated that a rather small aortic valve area can allow near-normal flow. It is our premise, therefore, that the diseased cusps of aortic stenosis can be partially resected, leaving a rim of firm tissue upon which the spring valve can seat. Toward this end, an aortic punch has been constructed to resect a standard opening in the stenotic aortic valve large enough to allow normal hemodynamics when covered with a spring prosthesis.

Summary

The fabrication of the aortic spring valve is described. The technique of insertion is demonstrated. Results over 20 months are encouraging. Resection of the stenotic aortic valve and replacement with a spring valve is considered feasible.

1401 Rivard St. (7) (Dr. Johnston).

DISCUSSION

Dr. B. Eiseman, Denver: I appreciate the opportunity of discussing this paper of Dr. Wible, inasmuch as we too have been working on the problem of aortic valve replacement for approximately two years. To date we have used about 15 types of prosthetic valves in more than 70 dogs.

Our technique involves placement of the subcoronary prosthesis via an open aortotomy, utilizing a pump oxygenator and coronary artery perfusion. At first we used a small side-arm from the oxygenator which was inserted into the coronary ostia, but this lies directly in the operative field, so that now we use retrograde coronary perfusion via the coronary sinus, a method which gives us ample time and good exposure. We routinely excise the aortic valves prior to placement of the prosthesis and therefore have good evidence of the function of the prosthetic valve.

We have experimented with many types of valves, a few of which we recently described at the A. C. S. Forum meeting. Collapsible conical valves and those seated within a plastic cage have been tried. The greatest difficulty, in our experience, has been in the thrombosis that occurs at the valve hinge. Since hearing Dr. Wible's original discussion of his experience with the watch-spring hinge at the College Forum, we have begun adapting this technique to some of our valves, and I can heartily endorse the efficacy of this ingenious device. I believe that this is an important contribution and that Drs. Wible, Jacobson, and Johnston are to be congratulated for their important work.

Dr. Egbert Howard Fell, Chicago: Dr. Wible and his associates from Detroit are to be complimented upon their very excellent presentation.

We have been interested in these problems for considerable time, and have watched the work of the Detroit group develop. It may be of interest if we go back to 1872, at which time Becker, who was an ophthalmologist, described a method of developing aortic insufficiency in the dog. He realized that aortic disease caused eye-ground changes. He took a long glass rod and went down through the carotid artery and disrupted the valves.

The problems of aortic disease, both stenosis and insufficiency, demand and are receiving great attention in the cardiovascular centers. It is only through consistent efforts such as those presented by Dr. Wible, and previously by Dr. Jordan, that these difficult problems will be solved. The prevention of acquired aortic disease is the fundamental desire of all, but, until that time comes, improved techniques for the surgical correction of aortic insufficiency and stenosis will be subjects of interest to cardiologists and cardiovascular surgeons.

Dr. James H. Wible, Detroit: I wish to thank the discussants for their very kind remarks. There are a couple of questions still left unanswered, at least, in our minds.

We are not certain that the amount of spring tension in the particular frame that we have been using is the proper one. We are in the process of trying to determine what would be the optimal spring tension that should be used.

Another question that is as yet unanswered is the effect that the diseased cusp of the host valve will have on the prosthesis when the flap seats against it. The diseased host valve is a hard, sometimes calcified, valve, and the question has come up in our mind as to whether this may affect the endothelial-like substance that grows out on to the prosthesis. We do not think it will, because the host valves in the animals do not appear to be altered over long periods of time. However, that is a question that is yet to be answered.

We feel that perhaps this prosthesis or some modification of this prosthesis may be applicable to the treatment of clinical aortic insufficiency.

REFERENCES

1. Hufnagel, C. A.: Surgical Treatment of Aortic Insufficiency, in Henry Ford Hospital Symposium on Cardiovascular Surgery, Philadelphia, W. B. Saunders Company, 1955.

2. Jordan, P., Jr., and Wible, J.: Spring Valve for Mitral Insufficiency, A. M. A. Arch. Surg. 71: 468, 1955.

3. Wible, J.; Jacobson, L. F.; Jordan, P., Jr., and Johnston, C. G.: Spring Valve Prosthesis for the Control of Valvular Insufficiency, S. Forum, to be published.

4. Cohen, M., and Lillehei, C. W.: Quantative Study of the "Azygos Factor" During Vena Caval Occlusion in the Dog, Surg. Gynec. & Obst. 98: 225, 1954.

5. Gorlin, R.; McMillan, I. K. R.; Medd, W. E.; Matthews, M. B., and Daley, R.: Dynamics of the Circulation in Aortic Valvular Disease, Am. J. Med. 18:855, 1955.

Role and Interpretation of Arteriograms in Atherosclerosis and Atherosclerotic Aneurysms

BEN EISEMAN, M.D., and HUBERT U. WAGGENER, M.D., Denver

Success in the direct surgical management of atherosclerotic peripheral vascular disease lies primarily in the proper selection of patients for operation.[1] Radiologic visualization of the diseased vessels ranks among the most important of the factors used in assessing candidates for such procedures. It is the purpose of this paper to delineate the role of arteriography in the diagnosis and surgical management of atherosclerotic peripheral vascular disease, on the basis of an experience in the radiologic visualization of the aorta and great vessels in a series of 134 patients with a atherosclerotic aneurysms and obliterative disease.

Materials and Methods

Radiologic visualization of the aorta or great vessels of the lower extremities was performed in a series of 134 patients during a three-year period immediately prior to October, 1956. During this time there were approximately twice this number of hospitalized patients examined for various manifestations of obliterative peripheral vascular disease in whom angiography was not considered indicated.

In this series of 134 patients, there were 33 patients with aneurysm and 101 patients with obliterative disease. In 57 cases the obliterative process was at or distal to the bifurcation of the common femoral artery. Abdominal aortography has been performed according to standard techniques,[2,3] utilizing local procaine anesthesia with the patient prone on the x-ray table. Tests for sensitivity to the dye are performed prior to the injection. A 10 cm. length of rubber tubing is inserted between the syringe and the aortogram needle to obviate displacement of the needle by movement of the syringe as injection is being performed under high pressure. The No. 15 aortogram needle is inserted into the aorta at the level of the 10th thoracic vertebra, and its proper placement is ascertained by a pulsatile flow of arterial blood from the needle when the stylet is removed. Thirty-five milliliters of saline is first injected under high pressure to make certain of the position of the needle. If the needle is not properly placed, the rapid injection of saline will produce immediate abdominal discomfort in the unanesthetized patient but will be of no serious consequence. If such saline injection is without incident, 30 ml. of 50% sodium acetrizoate (Urokon Sodium) is injected as rapidly as possible, and the exposure is made as the last 5 ml. of the solution leaves the syringe.

When visualization of the femoral vessels as well as the abdominal aorta is desired, a separate 36 in. casette is placed immediately inferior to the one used for visualizing the abdominal vessels and a portable 250 kv. machine is placed so as to visualize the entire thigh. Exposure of the thigh film is made two to three seconds later than the abdominal picture.

Visualization of the thoracic aorta has been performed a total of 18 times on 15 patients by a technique previously described[4] and has proved entirely satisfactory.

Femoral arteriography has been performed by the percutaneous injection of 20 ml. of 50% sodium acetrizoate into the common femoral artery through a No. 15 needle.

Complications of Arteriography

Aortography and arteriography is not a completely harmless procedure, and its hazards must be weighed against the benefits to be obtained by its use.

In this series the radiopaque dye has on occasion inadvertently been injected into an abnormally high renal artery, into the splenic artery, into the superior mesenteric artery, and into the celiac artery, but in no instance has the 50% sodium acetrizoate caused more than transient abdominal distress, and there have been no other serious sequelae. Early in this experience approximately 15 ml. of

Read at the 64th Annual Meeting of the Western Surgical Association, Cincinnati, Dec. 1, 1956.

From the Department of Surgery, University of Colorado School of Medicine, and the Denver Veterans Administration Hospital.

dye was injected into the periaortic region with resultant discomfort but, fortunately, without other damage. Since the routine injection of 35 ml. of saline into the aortogram needle prior to injection of the dye, such periaortic extravasation has occurred but once.

In one instance a patient with pancreatitis underwent an aortogram in order to rule out a splenic artery aneurysm. The aortogram was satisfactory, but following the study the patient went into shock, and at laparotomy there was blood in the peritoneal cavity, presumably from a lacerated spleen. Splenectomy was performed, but the patient ultimately died with a subdiaphragmatic abscess.

Femoral arteriography did not result in any serious sequelae, but on two occasions there was extravasation of the dye into the periarterial tissue and the resultant inflammatory reaction delayed operation through this site. In two other patients dye was injected into the femoral vein rather than into the artery. Although this was of no consequence, care must be taken not to interpret such venograms as abnormal femoral arteriograms, for occlusion of the vessel at the first competent venous valve in the thigh may resemble obstruction of the femoral artery at this point.

Postinjection spasm of the distal vessels has not proved to be of serious significance. In extremities of questionable viability 10 to 15 ml. of 50% sodium acetrizoate normally has been sufficient to outline the diseased vessel, and on occasion 1 ml. of 1% procaine hydrochloride has been mixed with the dye to minimize vascular spasm.

Aneurysms

Indications.—The diagnosis of most abdominal and peripheral arterial aneurysms can be made without their radiologic visualization.[5] Such studies, therefore, are indicated only for more accurate localization of their proximal and distal extent and to determine the diameter of the lesion—facts which on occasion alter the surgical approach and therefore warrant inclusion in the preoperative studies.

Most atherosclerotic aortic aneurysms arise almost immediately below the renal arteries and can be easily palpated by the time they become clinically significant. Their diagnosis and surgical extirpation are now well standardized,[6] and if operation is clearly indicated aortography would seem to be of no benefit. The occasional atherosclerotic aortic aneurysm that extends proximally into the lower chest must be recognized preoperatively and deserves complete aortographic study, since it requires an entirely different surgical approach.[7] Such an unusual proximal extension of the aneurysm can be suspected without routine aortographic visualization of every abdominal aneurysm.

The frequent occurrence of multiple atherosclerotic aneurysms[8] provides an added indication for radiologic visualization of the less-exposed segments of the arterial tree in a person with one evident aneurysm. Normally such multiple dilatations are clinically evident, but on one occasion an unsuspected aneurysm appeared in the common iliac artery at the site of a previous endarterectomy and ruptured into the sigmoid colon—a complication that might have been prevented if periodic follow-up aortograms had been performed.

Crane recently has suggested that the size of an aneurysm is of prognostic significance in determining its likelihood of rupture.[9] In his autopsy series aortic aneurysms of less than 6 cm. in diameter fatally ruptured in but 4% of the cases, whereas the remainder of the patients died of some other manifestation of atherosclerosis, such as coronary occlusion. He suggests that small aneurysms seldom rupture and need not necessarily be excised. These findings emphasize the importance of determining the diameter of small aortic aneurysms in order to determine the need for their removal. Since palpation is an inaccurate method of determining the size of such small aneurysms, their aortographic visualization seems indicated. In

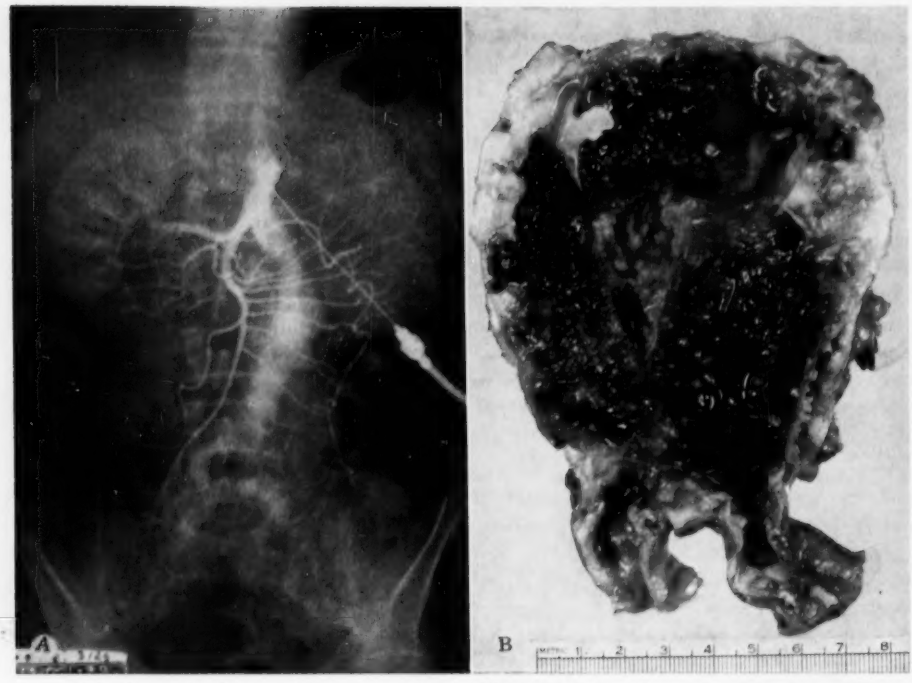


Fig. 1.—Abdominal aortic aneurysm showing discrepancy of (*A*) aortographic appearance and (*B*) open resected specimen.

one instance in this series an abdominal aortic aneurysm at first judged too small to warrant its resection was found on subsequent aortographic follow-up studies to have enlarged and was successfully resected. Our current policy is to visualize only the small aneurysms in poor-risk patients where a nonoperative management may be indicated.

Interpretation.—Although precise measurement of the diameter of an abdominal aortic aneurysm is desirable, comparison of the preoperative aortogram with the lesion at the time of surgery and the open resected specimen has often demonstrated a wide discrepancy between the specimen and its arteriographic profile.

Aneurysms are not thin-walled blood-filled sacs, but are composed of a varying number of concentric fibrotic peels, beneath which may be trapped a varying thickness of organized thrombus. On occasion the thrombus may be further perforated by areas of recanalization. It is obvious, therefore, that an intraluminal dye cannot routinely fill or visualize the entire aneurysm. In some cases only a thin central stream of dye will appear in a large, thick-walled, partially occluded aneurysm (Fig. 1). On other occasions the dye will flow through areas of recanalization or between two lamina of the thrombus, thus producing an irregular pattern that may be mistaken for the peripheral confines of the aneurysm.

Complete reliance cannot therefore be placed upon exact delineation of the contours of the aneurysm by angiographic techniques, since they result in a contour smaller by an unpredictable degree than the actual vascular lesion. Calcification within the wall of the aneurysm or the outline of a soft-tissue mass may indicate in a general way the diameter of the arterial dilatation, but neither indication is accurate, since calcific plaques may not be in the outer peel of the aneurysm wall.

The degree of organization of the thrombus may be of critical significance to the release of emboli and thus to the survival of the extremity distal to the aneurysm. No indication of the degree of such organization can be foretold by the radiographic findings. Thus, in two patients with peripheral arterial aneurysms that appeared very small and harmless on arteriographic studies loose emboli were dislodged from the aneurysms and irreversible distal gangrene resulted.

In atherosclerotic aneurysmal disease, therefore, radiologic visualization of the lesion is of most benefit when there is doubt as to the need for operative intervention or when an unusual or complicated aneurysm may exist.[10] Routinely, such studies are not necessary.

Arteriography in Obliterative Disease

The diagnosis of occlusive disease of the aorta, iliac arteries, and great vessels of the lower extremities normally can be established by history and physical examination and does not require radiologic visualization of the involved vessel.[11,12] Arteriography, however, may localize the point of maximal occlusion, delineate the peripheral extent of this process, and outline the collateral circulation around it, factors that to a major degree determine the surgical approach to the lesion and its anticipated chance of success. Such studies, therefore, are of greatest value in selecting patients for direct surgical procedures on the involved vessels.[13,14]

Indications.—The majority of patients suffering from peripheral arterial insufficiency have such obvious evidence of generalized obliterative disease[15] that they are not potential candidates for direct arterial surgery on the extremities or, therefore, for arteriographic study. More than two-thirds of the hospitalized patients in this series had such advanced coronary, renal, or cerebral disease that peripheral arteriography was contraindicated for this reason.

Any patient with obliterative arterial disease who, after thorough clinical study, is a reasonable candidate for direct arterial surgery should have arteriographic visualization of the involved vessels. Such studies may furnish accurate data as to the level of arterial occlusion, the length of the occlusive process, its degree of encroachment upon the lumen of the vessel, and the degree and location of collateral circulatory pathways and may indicate the condition of the vessels on both sides of the main occluding process. In an occasional case they will confirm or deny a diagnosis of obliterative disease that normally can be made on clinical grounds alone.

Of these factors, the condition of the arterial system distal to the point of the main obliterative process is clinically of most importance, since the degree of patency of these vessels is the major determinant in maintaining vessel or graft patency following direct surgical procedures.[1,16-19] Visualization of the distal vessels may be obtained on routine arteriography if there is only an incomplete obstruction of the vessel or if collateral channels fill the main arteries beyond a complete obstruction. Unfortunately, in atherosclerosis such filling by collateral channels is unusual because of obliterative changes in the distal portion of the vessel. Since nonvisualization of the vessel distal to a complete obstruction does not necessarily signify that an adequate vessel may not exist, surgical exploration of the distal vessels or distal operative arteriograms[20] are then indicated.

In this group of 134 cases, surgical exploration of the distal vessels (superficial femoral or popliteal artery) has precluded further surgery in 12 instances. In five other cases arteriography of the vessels distal to the main point of obstruction showed such evidence of diffuse peripheral disease that further futile surgical interference was avoided.

As clinical experience increases, fewer aortograms and arteriograms are being performed for obliterative arterial disease—a trend that is similar to the situation in angiocardiographic evaluation of operative

cardiac lesions. This raises the question of the justification for any such radiographic studies.

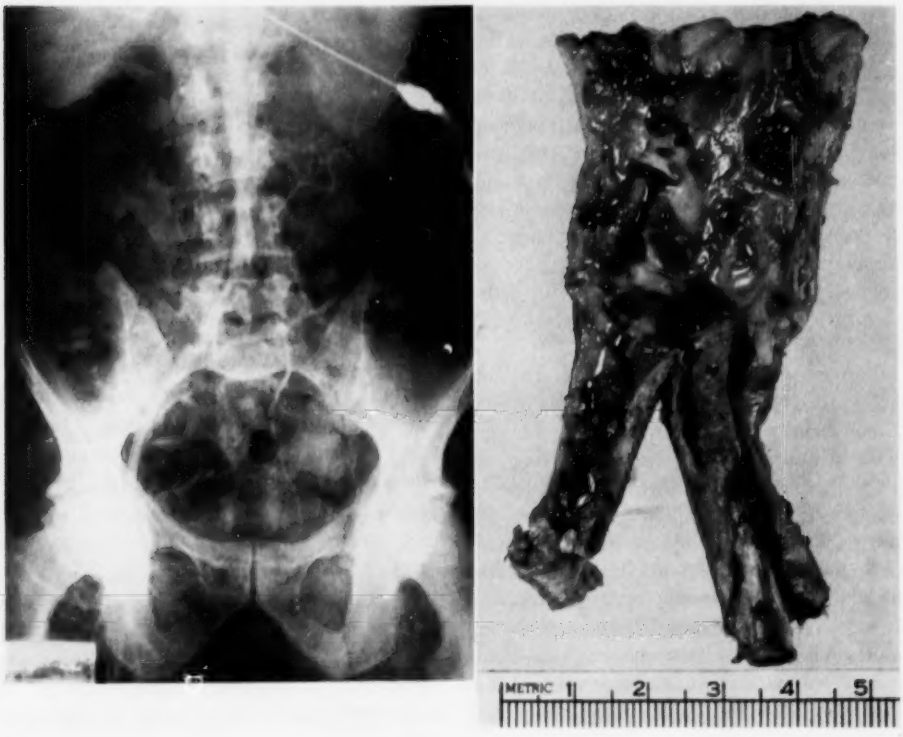
Although our use of angiography in obliterative disease is becoming more selective, in certain circumstances it is indicated. In some instances clinical evaluation leaves doubt as to the operability of the occlusive lesion, and arteriography may clarify the issue. More frequently, however, angiography is employed preoperatively in order to obtain the maximum information concerning the status of the lesion and the collateral vascular response to it. Surgical exploration of the distal vessels on occasion is more informative than angiography, and it is conceivable that such a technique will further limit the use of angiography in occlusive disease.

Interpretation.—Arteriography of the normal unobstructed vessel reveals a bright dye column with straight edges and homogeneous density: The point of bifurcation is sharp and clearly outlined.

Atherosclerotic changes first appear at or near a major bifurcation, where the artery is fixed to an unyielding adjacent structure or where the vessel is partially constricted at a flexion crease or by an overlying soft-tissue band. Advanced intimal proliferative changes occur at these points before there is clinical evidence of such disease.

Blood flow through a vessel remains relatively unchanged until the diameter of the vessel has been reduced approximately 70%.[21] Development of collateral vascular channels further delays the onset of clinical symptoms. Thus, by the time claudication

Fig. 2.—Atherosclerotic obliterative disease of abdominal aorta and common iliac vessels, demonstrating the discrepancy between clinical incapacitation and pathologic changes. Despite the extensive nature of the obliterative process this 42-year-old man had minimal claudication until a few weeks before entry into the hospital. Note irregular moth-eaten appearance of the narrowed abdominal aorta involved with advanced obliterative disease.



appears, occlusion of a major vascular channel is already at an advanced stage (Fig. 2). Angiographic evidence of such disease lags far behind the pathologic changes, but by the time there is clinical evidence of disease some arteriographic evidence is also present.

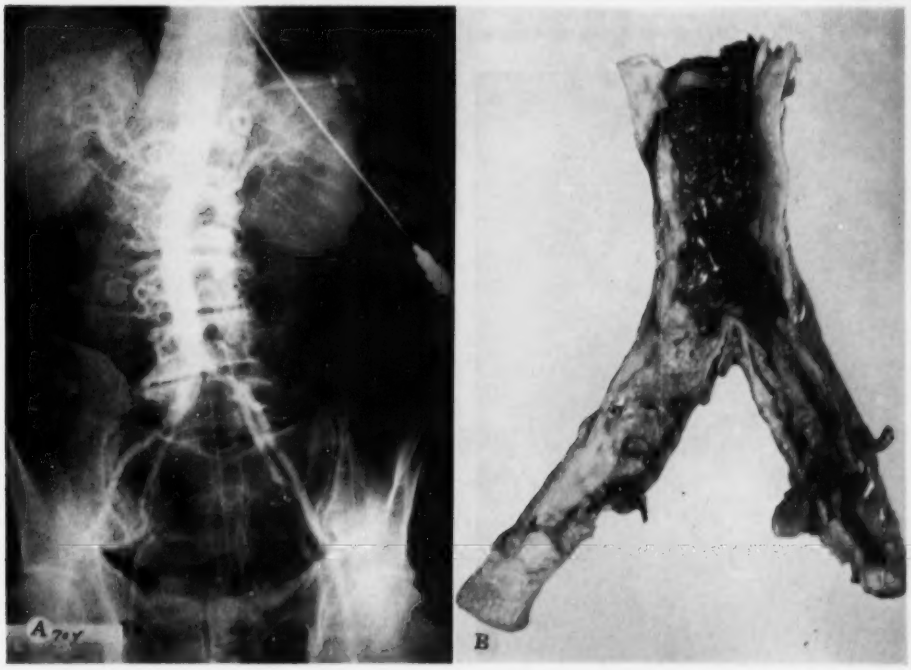
Blunting of the normally sharp outline of the "crotch" of a major arterial bifurcation and a slight radiolucency of the dye column along one limb of the vessel is usually the earliest arteriographic evidence of atherosclerotic obliterative disease. As the proliferative changes progress, a filling defect appears at the bifurcation and along one branch of the vessel. The other limb of the bifurcated vessel may appear completely normal.

Incapacitating symptoms of claudication commonly occur at this stage of the disease, even though the angiographic findings are singularly unimpressive. Initially it was difficult to believe that such minimal arteriographic changes represented an occlusive process sufficiently advanced to produce marked clinical symptoms. Surgical excision of these lesions demonstrated pathologic changes far more extensive than were anticipated from the arteriograms.

Cases with minor aortographic defects apparently limited to one side of the bifurcation routinely have been found at operation to have extensive proliferative changes in both iliac arteries. On occasion it was difficult to differentiate which of the two branches of the vessel was more involved, despite their markedly different angiographic appearance (Fig. 3). Regardless of the aortographic evidence, seldom, if ever, is there unilateral disease near a bifurcation.

Progression of atherosclerotic changes from their origin is toward further extension into the lumen of the vessel, toward circumferential involvement of the artery, or along the length of the vessel. Usually

Fig. 3.—Atherosclerotic changes at the aortic bifurcation showing (*A*) aortographic changes and (*B*) pathologic lesion. In this case the iliac artery less involved on aortography has the greater pathologic change. This demonstrates the fallibility of aortography in portraying the bilateral nature of the disease and its actual extent.



all three dimensional changes occur simultaneously but each is slow to become radiologically evident. Proliferative changes into the lumen may be hidden by a thin ribbon [14] of overlying blood, and the true extent of the underlying obstructive process may be almost totally masked. Similarly, a circumferential extension may remain hidden until the opposite wall of the vessel is involved and the profile of the process is revealed only as a slight filling defect. Since such proliferative changes normally first occur at the bifurcation of an artery, a niche or filling defect on the opposite or lateral wall of one of the arterial branches represents an extensive process that at least involves the entire posterior (fixed) portion of the vessel or is completely circumferential.

The linear extent of the obliterative process is of greatest clinical significance, for largely upon the segmental character of the lesion depends the success of surgical therapy. Unfortunately, the early longitudinal progress of an obliterative process is not radiologically evident. In small-caliber vessels, where the dye column is thin, such changes may be more obvious, but in large vessels, such as the aorta, the deep column of overlying blood obscures the process. The first evidence of intimal proliferation along the length of a major vessel is a series of irregular areas of radiolucency which give a moth-eaten look to the dye column (Fig. 2*A*. This untidy appearance may further be enhanced by small irregular filling defects along the profile of the vessel (Fig. 4).

Fig. 4.—Diffuse atherosclerotic changes involving the entire superficial femoral artery represented by an irregular moth-eaten appearance of the vessel, with narrowing and areas of decreased density of the dye.

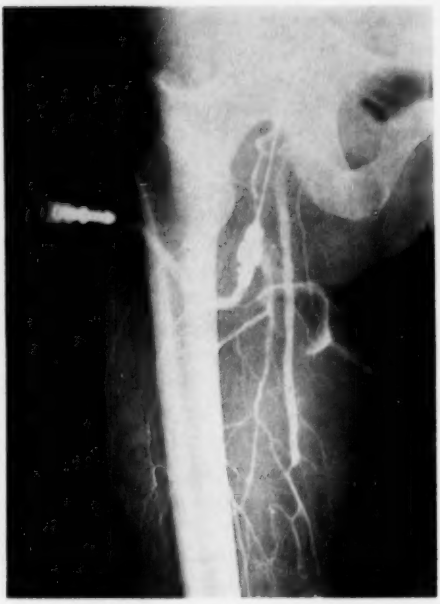


Fig. 5.—Femoral arteriogram showing an apparent proximal limitation of the obliterative process at the midthigh. The irregular contour of the vessel above this point actually indicated diffuse disease—a finding confirmed at operation. Although the vessel below the point of complete obstruction is not visualized on arteriography, it was found to be patent at operation.

The proximal limit of the atherosclerotic process usually is more extensive than is indicated by angiography. This is of particular importance in the surgical approach to obliterative disease in the femoral vessels, where the proximal end of a by-pass graft or endarterectomy must be performed above the segment of the obliterative process (Fig. 5). Unless the surgeon is aware of the fallibility of the radiographic tech-

niques, the proximal arteriotomy will be made into an area involved with marked atheromatous change, with compromise of the operative result. In occlusive disease of the aorta this is of less importance, since atherosclerotic plugs can be removed from the level of the renal arteries or even proximal to this point.

Reliable visualization of the distal obliterative process is even more difficult. When there is complete occlusion, collateral filling may not reveal the distal extent of the lesion (Fig. 5), but even when there is only partial occlusion the terminal end of the obstructive process is usually hidden beneath the turbulent flow distal to the point of maximum obstruction. Any arteriographic irregularity in the vessel or narrowing of the lumen distal to such an area of partial obstruction usually represents advanced obliterative disease. It is because of this discrepancy between the arteriographic image and the pathologic changes in the vessel that surgical exploration of the distal artery is routinely performed as the first part of the direct surgical approach to atherosclerotic obliterative disease when its segmental nature is in doubt. The obliterative process is infrequently as well localized as either the angiograms or the current surgical literature would have one believe!

Fig. 7.—Femoral arteriogram of a 32-year-old man with microscopically proven Buerger's disease in both upper and lower extremities. Note complete occlusion of superficial femoral artery, with visualization of distal segment via collateral vessels.

Fig. 6.—Aortogram of a 42-year-old man with microscopically proven thromboangiitis obliterans, showing advanced obliterative changes in the aorta.

Buerger's Disease

Eight male patients all less than 43 years of age with clinical signs and symptoms typical of Buerger's disease and with microscopic diagnosis of thromboangiitis obliterans had angiographic study of the major vessels of the lower extremities. In two patients there was advanced obliterative disease of the abdominal aorta (Fig. 6), and in two others the iliac and femoral vessels showed such involvement (Fig. 7), both on arteriography and at surgical exploration. Neither the radiographic studies nor the operative appearance of these lesions could be differentiated from those of typical atherosclerosis.

Buerger's disease, according to the accepted definition,[22] is characterized by

periarterial inflammation and involves the arterioles and small-caliber vessels. Atherosclerosis, on the other hand, characteristically involves larger vessels in a noninflammatory process. Angiographic and operative experience suggests that these features are limited neither to Buerger's disease nor to atherosclerosis, for the atherosclerotic vessel is characteristically surrounded by dense inflammatory reaction that involves the accompanying vein. The unexpected angiographic finding of large-vessel involvement in Buerger's disease further complicates the differentiation of these two disease processes.

Thus, neither the location of the disease nor the extent of the periarterial inflammatory changes can reliably separate these two angiopathies, and this suggests that their differentiation is not so simple as was previously supposed. As clinical experience increases, their separation becomes more difficult, and the question arises as to whether thromboangiitis obliterans and atherosclerosis do not represent two variants of the same disease.

Summary

The indications for and interpretations of arteriograms in atherosclerotic obliterative and aneurysmal disease are presented on the basis of studies in 134 such patients.

The diagnosis of atherosclerotic aneurysm normally can be made without its angiographic visualization, and such studies are now employed only when the indications for operation are in doubt or because of some other complicating factor.

Comparison of the angiographic profile of arterial aneurysms and their operative appearance emphasizes the limitations of the method in predicting the size of the aneurysm, the thickness of the thrombotic "pell," and the consistency of the contained thrombus.

The progressively more selective indications for angiography in obliterative arterial disease are discussed, and emphasis is placed on their use only when direct arterial surgery is contemplated.

The discrepancy between angiograms and the operative appearance of an atherosclerotic lesion emphasizes that marked pathologic changes occur prior to their angiographic appearance and that both the length of the obliterative lesion and the degree of luminal involvement characteristically are underestimated by such studies.

Angiographic and operative changes similar to those found in atherosclerosis were found in the major vessels of the lower extremities in four of eight patients with microscopically proven Buerger's disease. The implications of these findings for the differentiation of these two angiopathies are discussed.

Veterans Administration Hospital, 1055 Clermont St. (20).

DISCUSSION

Dr. Louis G. Hermann, Cincinnati: Dr. Eiseman's presentation is a very timely one and is worthy of further discussion. Here in Cincinnati we have also been cautious about the employment of arteriography in patients with extensive obliterative changes in the peripheral arteries.

We believe that simpler methods of diagnosis frequently will give us adequate information about the location and extent of arterial obliteration and thus enable us to institute satisfactory treatment. There are many inherent dangers associated with both aortography and peripheral arteriography, and many lives and limbs are sacrificed each year because of complications which are directly related to the introduction of the radiopaque medium into diseased blood vessels. We agree with Dr. Eiseman about the difficulty of interpreting many of the arteriograms, and we have been convinced for many years that this method of study does not give us accurate information about the functional activity of the collateral arterial pathways and, in many instances, does not show the collateral arterial pathways in their full anatomic distribution. Dr. Eiseman has again cautioned all of us about the shortcomings and the dangers inherent in the method, and we would do well to consider them seriously.

Dr. Eiseman used the term "thromboangiitis obliterans" in a general way rather than in the specific sense in which Leo Buerger originally meant it. We are convinced that the active angiitis which we see predominately in young men is different from, and not an early stage of, the degenerative arterial diseases. Some years ago we reproduced the classical pathologic change in the arterioles of the tail and digits of white rats by

feeding them ergot preparations of various types. Thromboangiitis as observed in young men of the Middle European countries has many of the clinical characteristics of endemic ergotism.

There is some cellular infiltration in the walls of large arteries of patients with both atherosclerosis and the type of medial sclerosis of major arteries described by Monckeberg; so, secondary thrombosis may occur at any point along the course of a major artery if the reaction in the wall of the artery is of sufficient intensity. I do not believe that the pathologic changes under such conditions are the same as those seen in true thromboangiitis obliterans, as Buerger described the entity.

We should all give serious thought to these problems and help find better means of evaluating the peripheral arterial circulation in patients with arteriosclerosis obliterans.

DR. WILLIAM S. DYE, Chicago: I enjoyed Dr. Eiseman's paper very much, because he has previously called our attention to the hazards of operating on all of these patients with aneurysms and occlusive disease.

We have learned in reverse, I must say, about angiography, in that we were not conservative in our approach and used angiography frequently, and as time has gone on, we have found that in many of these cases exploration actually decided what was to be done.

REFERENCES

1. Eiseman, B.; Rainer, W. G.; Malette, W. G., and Huffman, E. R.: Indications for Direct Arterial and Aortic Surgery in Obliterative Disease, A. M. A. Arch. Surg. 73:411-417 (Sept.) 1956.

2. Melick, W. F., and Vitt, A. E.: The Present Status of Aortography, J. Urol. 60:321-334 (Aug.) 1948.

3. Julian, O. C., and Dye, W. S.: Arteriography, S. Clin. North America 35:275-284 (Feb.) 1955.

4. Eiseman, B., and Rainer, W. G.: A New Technique for Thoracic Aortography Using the Right Supraclavicular Approach, A. M. A. Arch. Surg. 71:859-862 (Dec.) 1955.

5. Estes, J. E.: Abdominal Aortic Aneurysm: Study of 102 Cases, Circulation 2:258-264 (Aug.) 1950.

6. DeBakey, M. E.; Cooley, D. A., and Creech, O., Jr.: Treatment of Aneurysms and Occlusive Disease of the Aorta by Resection: Analysis of 87 Cases, J. A. M. A. 157:203-208 (Jan. 15) 1955.

7. DeBakey, M. E.; Creech, O., Jr., and Morris, G. C., Jr.: Aneurysm of Thoracoabdominal Aorta Involving the Celiac, Superior Mesenteric, and Renal Arteries: Report of 4 Cases Treated by Resection and Homograft Replacement, Ann. Surg. 144:549-573 (Oct.) 1956.

8. Lesser, A.: Bilateral Femoral Aneurysms, New York J. Med. 56:2269-2271 (July 15) 1956.

9. Crane, C.: Arteriosclerotic Aneurysm of the Abdominal Aorta, New England J. Med. 253:954-958 (Dec. 1) 1955.

10. Eiseman, B., and Hughes, R. H.: Repair of an Abdominal Aortic Vena Caval Fistula Caused by Rupture of an Atherosclerotic Aneurysm, Surgery 39:498-504 (March) 1956.

11. DeBakey, M. E.; Creech, O., Jr., and Cooley, D. A.: Occlusive Disease of the Aorta and Its Treatment by Resection and Homograft Replacement, Ann. Surg. 140:290-310 (Sept.) 1954.

12. Crawford, E. S.; Creech, O., Jr.; Cooley, D. A., and DeBakey, M. E.: Treatment of Arteriosclerotic Occlusive Disease of the Lower Extremities by Excision and Graft Replacement or By-Pass, Surgery 38:981-992 (Dec.) 1955.

13. Julian, O. C.; Grove, W. J.; Dye, W. S.; Olwin, J., and Sadove, M. S.: Direct Surgery of Arteriosclerosis, Ann. Surg. 138:387-403 (Sept.) 1953.

14. Dye, W. S., Jr.; Olwin, J. H., and Julian, O. C.: Further Considerations on the Indications for and Limitations of Direct Surgery in Arteriosclerosis, Circulation 8:708-714 (Nov.) 1953.

15. Huffman, E. R.; Beckwith, R.; Blount, S. G., and Eiseman, B.: The Association of Generalized Atherosclerosis with Obliterative Disease of the Abdominal Aorta and Great Vessels of the Lower Extremities, to be published.

16. Warren, R.: Recent Advance in the Surgery of Arterial Disease, Veterans Administration Technical Bulletin, pp. 12-13, Sept. 15, 1955.

17. Hoye, S. J., and Warren, R.: Follow-Up Studies of Ileofemoral Arterial Reconstruction in Arteriosclerosis Obliterans, New England J. Med. 254:102-106 (Jan. 19) 1956.

18. Humphries, A. W.; de Wolfe, V. G., and LeFevre, F. A.: Analysis of 120 Consecutive Cases of Major Arterial Grafts, J. A. M. A. 161:953-956 (July 7) 1956.

19. DeBakey, M. E., and Cooley, D. A.: Surgical Considerations of Acquired Diseases of the Aorta, Ann. Surg. 139:763-777 (June) 1954.

20. Barker, W. F.: Distal Operative Angiography as an Aid in Endarterectomy, Surgery 36: 233-236 (Aug.) 1954.

21. Kunkel, P., and Stead, E. A., Jr.: Blood Flow and Vasomotor Reactions in the Foot in Health, in Arteriosclerosis, and in Thromboangiitis Obliterans, J. Clin. Invest. 17:715-723 (Nov.) 1938.

22. Allen, E. V.; Barker, N. W., and Hines, E. A.: Peripheral Vascular Disease, Philadelphia, W. B. Saunders Company, 1946, Ch. 17. Thrombo-Angitis Obliterans, pp. 405-406.

Replacement of Long and Narrow Arterial Segments

II. Experimental Studies with an Elastic ("Helanca") Seamless Woven Nylon Prosthesis

D. EMERICK SZILAGYI, M.D.; JOHN G. WHITCOMB, M.D., and CLAIBOURNE P. SHONNARD, M.D., Detroit

We have previously reported that seamless woven tubes of nylon or Teflon (a plastic consisting of tetrafluoroethylene polymer), 7-10 mm. in diameter and 18-24 cm. in length, function well as experimental arterial substitutes in anatomical locations where they are not subjected to bending stress.[1] When bent, these tubes buckle and show a high incidence of wrinkle thrombosis. Since it appeared that a prosthesis with elastic qualities would overcome this deficiency, our attention was turned to a prosthesis composed partly of an elastic nylon yarn.

Materials and Method

Characteristics of the Prosthesis.—The prosthesis used is woven with an ordinary tubular weave as a seamless tube and is made up of two types of nylon yarn. A magnified view of this material is shown in Figure 1. The longitudinal fibers are so-called "Helanca" nylon, and the circular fibers are plain, straight nylon. Table 1 gives the details of the weave, the thread count, and the type of nylon used for the circular filling.

"Helanca" refers to a patented process whereby nylon fiber is twisted into a tight spiral and then this twist is heat-set at 270 F. Two plies with opposite twists are combined to make the final yarn. The yarn actually stretches by uncurling, while the two plies with opposite twist counterbalance each other to give a stable yarn. Figure 2 compares the flexion wrinkling characteristics of similarly fabricated, seamless tubes woven of Orlon, Teflon, and the Helanca and nylon combination.

The finished plastic tube, which has been boiled in soapy water to shrink the Helanca fibers and make them more resilient, has an ability to elongate 15%-20%. The pH of the freshly woven tube, when soaked in distilled water, averages 6.6. Rinsing several times in distilled water or isotonic saline does little to change this.

TABLE 1.—*Textile Characteristics of Helanca Nylon Prosthesis*

Diameter of Prosthesis, Mm.	Ends (Warp)	Helanca Nylon	Picks (Woof)	Filling * (Woof)
7	55	70/2	80	210 nylon
8	63	70/2	80	210 nylon
9	71	70/2	80	210 nylon
10	79	70/2	80	210 nylon

* The filling (or circular) yarn is ordinary (Type 66) nylon, with the following characteristics: 210 denier, Type 300-5 turn, Z twist, 34 filament.

It is possible to cut this material with a heated niochrome wire or a cautery of the cutting-diathermy type. Sterilization is accomplished either by boiling or with chemical sterilizing agents. The prostheses placed in experimental animals were boiled; clinical cases received prostheses sterilized with a 24-hour immersion in 1:1000 aqueous benzalkonium chloride U. S. P. (Zephiran chloride) solution. The graft is cleared of benzolkonium with a double rinse of sterile saline.

Surgical Technique.—Prostheses 7-10 mm. in diameter and 13-15 cm. in length, of the composition just described, were implanted in 23 healthy male mongrel dogs weighing 8-20 kg. as an aortic by-pass with the following technique:

Under semiclosed, ether-oxygen anesthesia with endotracheal intubation, the left chest and flank of the normothermic dogs were shaved, surgically prepared, and draped in continuity. Using the preparation of McCune and Blades,[2] the left chest was entered through the eighth interspace, and the abdominal aorta was exposed through a left lumbar retroperitoneal approach (Fig. 3). During the open thoracotomy a mechanical respirator was used. The distal anastomosis at *B*, between the distal end of the obliquely cut Helanca tube and the side of the abdominal aorta well below the level of the renal vessels, was first performed. Blunt dissection then created a retrodiaphragmatic and retropleural tunnel for the passage of the proximal end of the prosthesis into the left chest. At

From the Department of Surgery, the Henry Ford Hospital, Detroit.

Supported in part by a grant from the Michigan Heart Association.

Read at the 64th Annual Meeting of the Western Surgical Association, Cincinnati, Dec. 1, 1956.

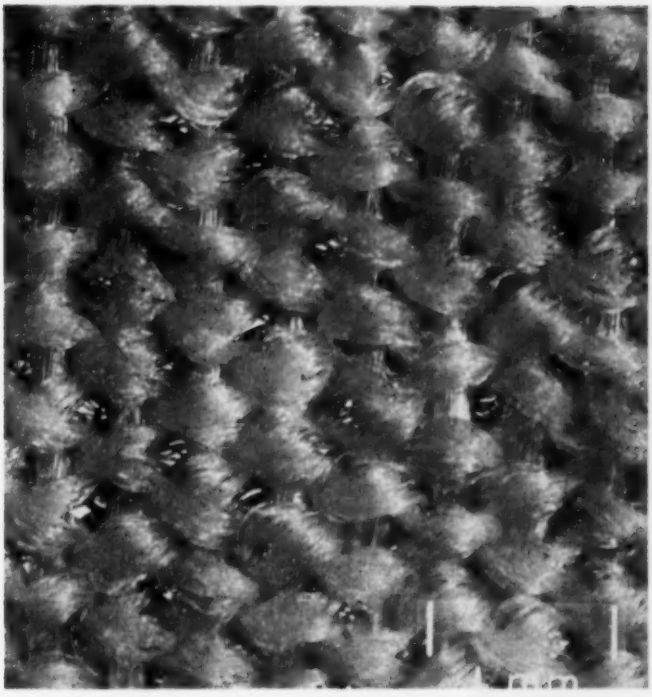


Fig. 1.—Surface view of taffeta weave with Helanca nylon. The strands of yarn running vertically in the photograph are of conventional nylon; these are the circular component of the prosthesis. The strands of yarn at right angles to the plain nylon, and having a fluffy appearance, are of Helanca nylon; these are the longitudinal component of the prosthesis (or the warp of the fabric). Reduced to 53% of mag. × 47.

the chosen level (Th 8 or Th 9) the thoracic aorta was cut across and an end-to-end anastomosis (*A*) was quickly performed between the proximal end of the prosthesis and the proximal stump of the thoracic aorta. The distal stump of the cut aorta was sewn over in two layers. Nonabsorbable surgical suture U. S. P. 5-0 (arterial silk) on Atraumatic needle was used as a continuous, over-and-over suture for the lateral anastomosis. Most of the implants were placed with enough redundancy to produce a tortuous course and thus create circumstances favorable to kinking. All dogs received intramuscular antibiotics for the first three postoperative days. Heparin was given only at the time of cross clamping the thoracic aorta.

This procedure is time-consuming and traumatic and carries a high immediate operative mortality, especially while the technique is being mastered. Only dogs surviving the first 48 hours of the postoperative period are considered in this report. All the animals that succumbed during the first 48 postoperative hours were autopsied, and none was found to have died of graft failure.

Frequent, periodic observations were made regarding the general condition of the host and the quality of the pulses distal to the prosthesis. The state of the implants was followed with interval aortography by percutaneous transthoracic left ventricular injection of approximately 8-10 ml. of 70% sodium acetrizoate (Urokon sodium). The intervals at which the animals were killed were as follows: 5, 10, and 20 days; 2, 4, 5, 6, 9, and 12 months. Agonal aortograms at the time of killing were obtained through a left thoracotomy by direct injection into the thoracic aorta. All prostheses were removed and their gross characteristics noted and recorded. Appropriate photographs and microscopic sections were taken. The tensile-strength characteristics of the prostheses were determined with the Instron instrument.* With normal fresh dog aorta and samples of new, unused prosthesis serving as standards, representative specimens recovered at 2, 6, 9, and 12 months were tested. Identical dumbbell-shaped samples were cut with a die in the longitudinal axis of the prosthesis, with a central or test area ½ in. in width. The rate of pull was constant, at 1 inch per minute. It was elected to test the full thickness of the wall of the recovered graft, for it is the combination of the prosthesis and its fibrous tissue sheath that replaces the artery and withstands the stress.

* The Instron instrument incorporates a highly sensitive electronic weighing system employing bonded-wire strain gauge for detecting and recording the load applied to the sample under test. Mr. W. D. Brown, Chrysler Corporation, Engineering Division, Detroit, and his associates assisted us with the measurements.

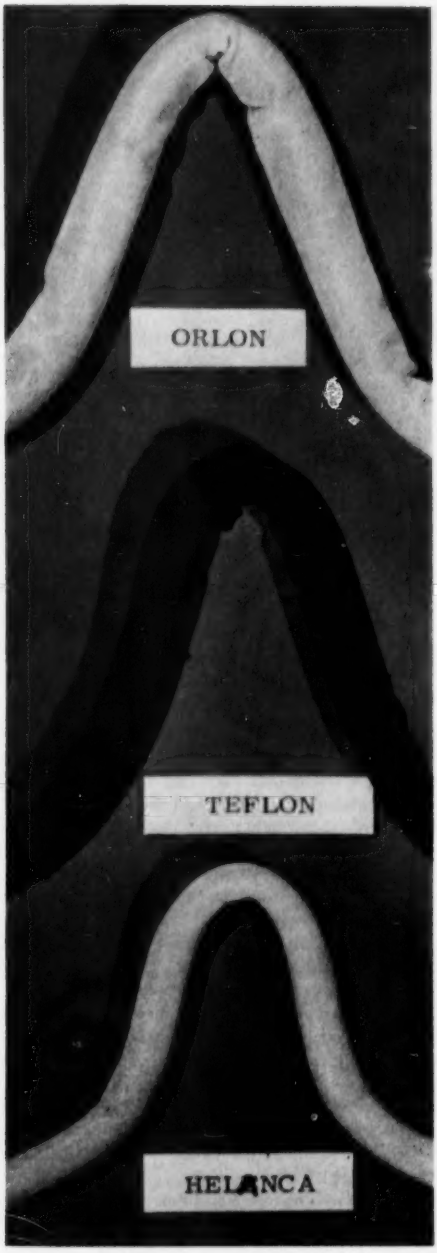
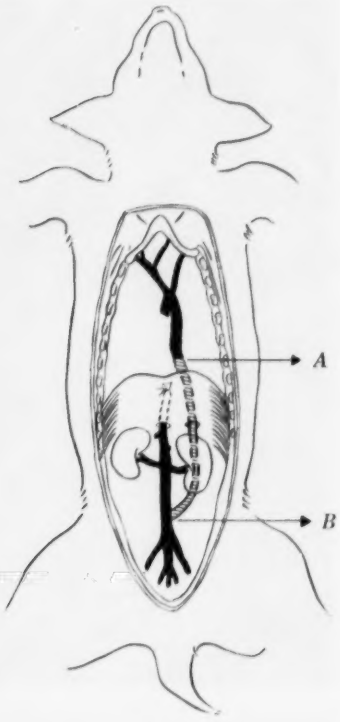


Fig. 2.—Comparative wrinkling characteristics of similar fabrics made of Orlon, Teflon, and Helanca nylon yarn.

Nine surviving dogs are being kept for long-term follow-up.



a

Fig. 3.—Experimental preparation: *A*, proximal; *B*, distal anastomosis. Modified from Figure 1 in article by W. S. McCune and B. Blades in *Annals of Surgery* (134:769, 1951), published by J. B. Lippincott Company, Philadelphia.

Results

For the evaluation of the performance of the implants in the 14 animals that were killed, functional capacity, aortographic appearance, necropsy findings, and tensile-strength determinations were studied and correlated (Table 2). All of the animals maintained a normal femoral pulse up to the day of death, and none died as a result of a graft failure. Five animals died of causes unrelated to the function of the implants. One of these dogs (No. 5, Table 2) succumbed to a disruption of the medial aspect of the distal anastomosis at four months. The disruption was on the aortic side of the anastomosis, the medial suture line having torn free, detaching a narrow longitudinal strip of aorta. The damage and

TABLE 2.—*Experimental Study of Long and Narrow Arterial Substitutes (Helanca)*

Series No.	Length of Follow-Up	Length of Graft, Cm.	Diameter of Graft, Mm.	Fate of Host	Autopsied Specimens			Comments
					Aortogram	Reaction Around Graft *	Luminal Surface	Results	
1	5 days	14	7	Died	None	0	0	Satis.	Empyema
2	10 days	14	7	Died	Unsatis.	+	Patchy	Satis.	Wound separation
3	20 days	13	7	Died	None	+	Patchy	Satis.	Empyema
4	2 mo.	14	10	Died	None	+	Patchy	Good	Neg. autopsy
5	4 mo.	14	7	Died	None	++	Patchy	Good	Rupture of distal aorta
6	5 mo.	14	9	Killed	Patent	++	I and S†	Good	
7	6 mo.	13.5	7	Killed	Patent	++	I and S	Good	
8	6 mo.	13.5	8	Killed	Patent	++	I and S	Good	
9	6 mo.	13	7	Killed	Unsatis.	+++	I and S	Good	Fib. plaque at diaph.‡
10	6 mo.	14	10	Killed	Unsatis.	++	I and S	Good	
11	6 mo.	13	10	Killed	Patent	++	I and S	Good	
12	6 mo.	13	9	Killed	Patent	++	I and S	Good	
13	9 mo.	13.5	7	Killed	Patent	++	I and S	Good	
14	12 mo.	15	7	Killed	Patent	+	I and S	Good	Makes two sharp curves; diastasis of sev. pcs. of yarn; no aneurysm

* Adventitial reaction (arteriogenesis): +, very thin layer of exudate; ++, less than 1 mm. thick; +++, more than 1 mm. but less than 3 mm. thick; ++++, more than 3 mm. thick.
† I and S: Intact and smooth.
‡ Fib. plaque: fibrous tissue plaque in lumen.

ultimate necrosis of the aortic wall had undoubtedly been caused by the occluding clamp.

The nutritional state of the animals remained good during the observation period. This fact is of particular significance when one considers that all of the blood going to the abdominal viscera is shunted through the by-pass and gains access to the upper abdominal aorta by retrograde flow.

None of the serial or agonal aortograms revealed occlusion, stenosis, aneurysm, or plaque formation in the prostheses in the 14 animals that came to autopsy. Numerous

Fig. 4.—Agonal aortogram (Dog 7; Table 2). Helanca nylon prosthesis six months after implantation (arrow at proximal anastomosis).

Fig. 5.—Agonal aortogram (Dog 14; Table 2). Helanca nylon prosthesis 12 months after implantation. The prosthesis, by design, follows a meandering course.

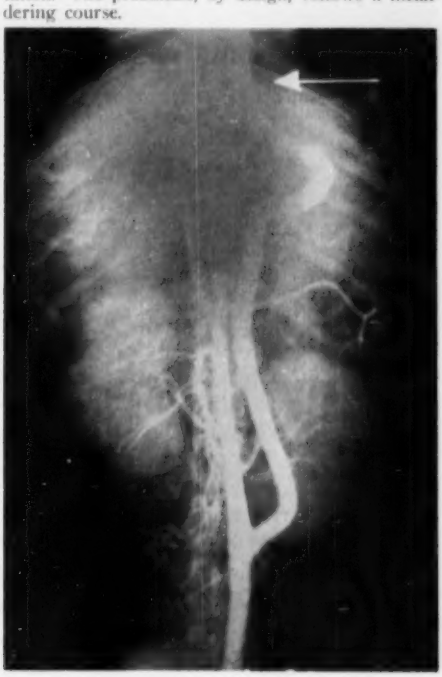


Fig. 6.—Appearance of luminal surface of H-N (Helanca nylon) prosthesis removed six months after implantation (Dog 7; Table 2, Fig. 4). Wall of moderate thickness. Luminal surface covered with intact smooth pseudointima.

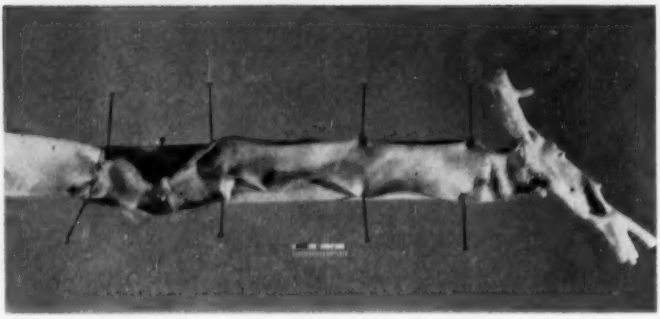


Fig. 7.—Appearance of luminal surface of H-N prosthesis removed 12 months after implantation (Dog 14; Table 2, Fig. 5). Ulceration of the intima in the dome of the sweeping curve of the implant (cf. Fig. 5), disclosing the underlying plastic fabric, was caused by the jet effect of the blood stream.

implants traversed sharp curves, with no evidence of kinking or wrinkling. The two types of anastomosis have also been free of progressive narrowing (Figs. 4 and 5).

The gross appearance of the 14 prostheses removed at autopsy was most satisfactory. The bed of surrounding connective tissue was orderly and free from gross inflammatory changes. The fibroblastic growth appeared to have gained easy ingress through the moderately porous weave of the prosthesis, and gave good support to the thin, smooth, pale-pink, glistening pseudointima which covered the full length of the implants six months or more of age (Figs. 6 and 7). An interesting variation on this pattern was seen with a prosthesis which was so placed in the retrodiaphragmatic tunnel as to come in direct contact with exposed skeletal muscle. At autopsy these areas showed greater adherence between the surrounding connective tissue and the muscle, and the inner lining was much thicker, but still orderly and purposeful.

Microscopic examination showed the cellular infiltrate of the round-cell type about the yarn to be moderately heavy. It was no more than that seen with conventional nylon prostheses but definitely in excess of that elicited by Teflon (Fig. 8). By 12 months it had decreased slightly and was more peripheral (Fig. 9).

The studies on tensile strength yielded interesting findings (Fig. 10). The normal fresh canine thoracoabdominal aorta was found to have a tensile strength of 12.5 lb. per 0.5 in. The prosthesis used in this study showed an initial tensile strength of 64 lb. per 0.5 in. of tested material. A striking decrease in tensile strength was seen during even the first two months of implantation. This was irregularly progressive up to the 12th month. At two months the tensile strength of the prosthesis and the surrounding connective tissue was 7 lb. per 0.5 in., and at 12 months it had decreased to 4.3 lb. per 0.5 in. In one instance in which a portion of the specimen was tested intact and another portion without the connective tissue sheath laid down in the process of arteriogenesis, the prosthesis was found to contribute only one-

Fig. 8.—Photomicrograph of section through the midportion of a H-N prosthesis recovered at six months (Dog 7, Table 2). Good pseudointima (top). Only moderate inflammatory exudate in the connective tissue in and outside the fabric. The connective tissue ingrowth is adequate. Hematoxylin and eosin; reduced to 79% of mag. × 50.

third of the total strength. The results of these tests are summarized in Figure 10.

Blood pressure determinations were obtained at the time of killing on some of the animals with a strain gauge and a direct-writing oscillograph (Fig. 11). Recordings were made below the graft, in the graft, and at several levels in the thoracic aorta above the graft.

The nine dogs that comprise the long-term survivors' group and have been followed for 7 to 12 months are in a good state of health and nutrition and have distal pulses in the femoral region. Each dog has had a recent aortogram which shows the graft to be patent and free of stenosis (Table 3). At the present it is planned to observe these dogs for two to five years.

Comment

A previous report of long and narrow arterial prostheses of nylon and Teflon implanted with the same technique as that here described gave excellent results from the

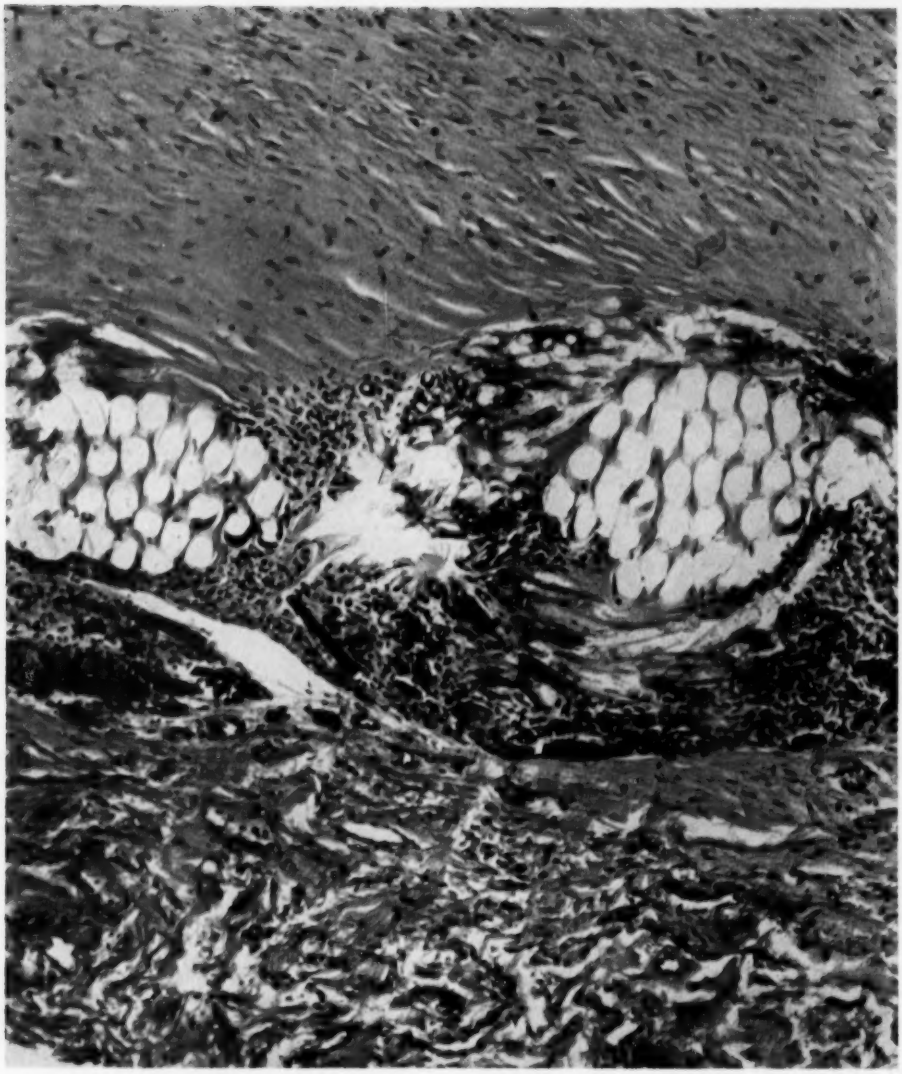


Fig. 9.—Photomicrograph of section through midportion of H-N prosthesis removed 12 months after implantation. Thick, moderately cellular, and intact pseudointima. Round-cell infiltration fairly heavy near the fabric but only mild on the outside. Connective tissue ingrowth active and orderly. In general, very satisfactory arteriogenesis. Reduced to 79% of mag. × 175.

point of view of tissue acceptance and satisfactory results with respect to the rate of postoperative thrombosis. Moreover, when thrombosis did occur, it was due almost entirely to wrinkling caused by a bending stress on the rigid, unyielding wall. This quality of lack of elasticity of all the heretofore available textile fabrics is a serious shortcoming, and has limited the clinical use of the prostheses made of them to the replacement of short arterial segments in anatomical locations where they are not subject to flexing. The elastic property of Helanca nylon yarn seemed to us to give

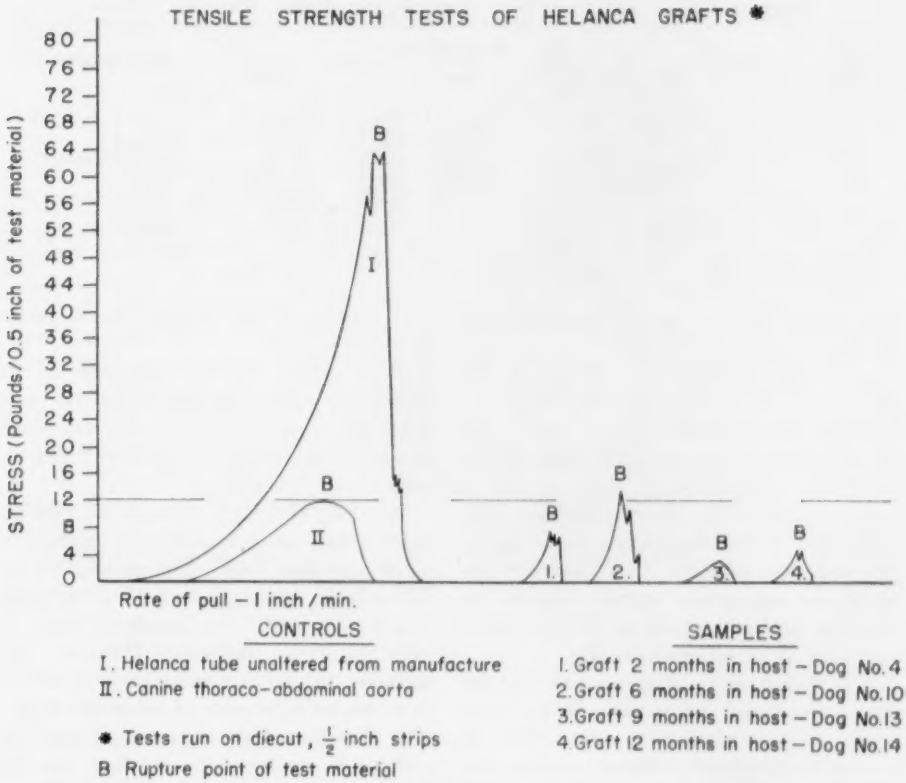


Fig. 10.—Tensile-strength curves on Instron instrument. (See also text.)

promise of overcoming this difficulty. It may be added that the exceptional durability and tissue acceptance of Teflon would have made it highly desirable to impart to it elasticity by chemical or physical processing; until now, however, this goal has not been possible to achieve.

Since elongation of the plastic textile tube in its longitudinal axis seemed to be the essential quality to prevent buckling, and since elongation in the transverse diameter seemed to create an undesirable ballooning effect, it was assumed that the Helanca yarn would best serve as the warp of the fabric. Observation of the behavior of the prosthesis after implantation bore out the correctness of this assumption. Circumferential elasticity is apparently not essential for

Fig. 11.—Blood pressure recordings with strain gauge and oscillograph. Marked alteration of pulse wave across prosthesis. (See also text.)

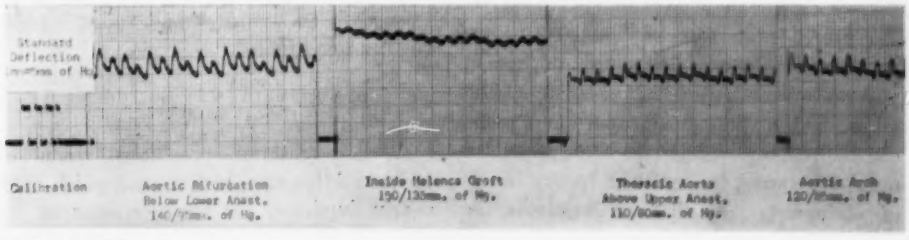


TABLE 3.—*Experimental Study of Long and Narrow Arterial Substitutes (Helanca)*

Series No.	Length of Follow-Up, Mo.	Length of Graft, Cm.	Diameter of Graft, Mm.	Living Specimens Fate of Host	Aortogram	Distal Pulses	Nutritional Status
1	12	14.5	7	L and W *	Patent	Good	Thin
2	10	14.2	7	L and W	Patent	Good	Fat
3	9	13	7	L and W	Patent	Good	Normal
4	9	13.5	9	L and W	Patent	Good	Firm and muscular
5	8	15	10	L and W	Patent	Excellent	Perfect
6	8	14	9	L and W	Patent	Excellent	Perfect
7	7	14	9	L and W	Patent	Good	Normal
8	7	13	9	L and W	Patent	Good	Normal
9	7	14	9	L and W	Patent	Good	Perfect

* L and W: Living and well.

maintaining the anatomical accommodation of the implant. The ability to elongate 15%-20% longitudinally is sufficient to permit the prosthesis to adjust its disposition according to the needs of its course and the movements of the adjacent parts. Moreover, even lengthwise elasticity is only a temporary necessity; after the implant is incorporated in the surrounding tissue bed, it does not tend to kink. Thus, although the fibroblastic ingrowth eventually dampens the elastic quality of the impant, this loss does not bring about untoward results.

It is important to bear in mind that the elastic quality of the Helanca nylon prosthesis, or, more precisely, its ability to elongate longitudinally without becoming deformed, is not identical with the elasticity of a normal artery. The lack of transverse elasticity markedly alters the pulse wave in the prosthesis, as shown by the strain-guage recordings. The lack of lateral yield apparently also raises the blood pressure within the prosthesis. These properties of the implant do not, however, seem to be harmful.

A brief comment on the evaluation of the functional state of the prosthesis is in order. In the experimental preparation used, complete occlusion of the implant leads to prompt death. In all live animals, therefore, the presence at least of a partially open graft may be assumed. Stenosis of various degrees of the prosthesis leads to malnutrition and possible death from intercurrent causes. Minor defects in the prosthesis must, of course, be searched for by means of angiography. By all these standards, the performance of the implants has been entirely satisfactory.

With regard to the acceptance of the Helanca prosthesis by the tissues, its tissue reactivity is similar to that of conventional nylon. It elicits appreciably more tissue reaction than Teflon does.

The loss in tensile strength of Helanca nylon fabric after implantation appears to be an important fault. Numerically, the decrease looks significant and of a magnitude that would render the prosthesis liable to early aneurysm formation. However, aortography and autopsy failed to show defects or weakness suggestive of aneurysm or diffuse dilatation. This apparent paradox can perhaps be explained by recalling that the tensile strength of the nylon fiber before implantation is in an enormous excess of the physiological need of the dog. It is probably safe to say that the normal dog's aorta has a fivefold margin of safety; the tensile strength of the Helanca fabric surpasses this five times. Thus, even after having lost 80% of its original tensile strength, the implant is still firm enough to meet the physiological demands placed on it. Its ability to maintain structural integrity is further bolstered by the development of its connective tissue investment. Nevertheless, the problem of the loss of tensile strength is an important one, and it is being further investigated.

Summary

A new arterial prosthesis made of Helanca nylon yarn is described which more nearly duplicates the characteristics of the

human artery. It is woven, seamless, smooth-walled, soft, and easy to handle and has longitudinal elasticity.

Among 23 implants, 7-10 mm. in diameter and 13-15 cm. in length, placed into the thoracoabdominal cavities of dogs as a proximal exclusion of the abdominal aorta, there were no failures. Gross and microscopic examination of 14 recovered implants showed excellent arteriogenesis of satisfactory tissue reactivity. Nine dogs with such implants are surviving in good health with angiographically normal prostheses after periods of observation up to 12 months.

Although tensile-strength determinations on the implanted specimens reveal a significant and progressive decrease soon after implantation, this loss has not produced demonstrable gross changes in the prostheses.

NOTE: On the grounds of the satisfactory results of these animal experiments, during the past four months we have used the Helanca nylon prosthesis in 10 clinical cases of occlusive arterial disease. Two of these cases were instances of common iliac, and eight were those of femoral, occlusion. One prosthesis, used as a femoral by-pass in a case of homograft failure, became thrombosed in the immediate postoperative period; the other nine implants have remained open both by clinical signs and by angiography during periods of observation of from two weeks to four months.

The tubular Helanca nylon prosthesis was supplied by Mr. John B. Sidebotham, Philadelphia.

Henry Ford Hospital (2).

REFERENCES

1. Szilagyi, D. E.; Shonnard, C. P.; Lopez y Lopez, J., and Smyth, N. P. D.: Replacement of Long and Narrow Arterial Segments, Surgery 40:1043, 1956.

2. McCune, W. S., and Blades, B.: Viability of Long Blood Vessel Grafts, Ann. Surg. 134:769, 1951.

Carotid Angiography in Diagnosis and Treatment of Tumors of the Neck

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Tumors of the neck may present difficult diagnostic problems. This may be especially true if the mass appears to involve the carotid vessels. Information as to the type of tumor and its relation to the carotid vessels may be obtained by use of carotid angiography. These considerations have recently been called to the attention of my colleagues and myself by two patients with grossly similar, pulsating tumors in the superior triangle of the neck.

Cerebral angiography was first introduced by Moniz in the late 1920's and since has been employed extensively for the investigation of intracranial tumors and cerebrovascular disease. The technique of the procedure has been well standardized and at present is a relatively safe procedure. We believe that carotid angiography is of particular value in cases of carotid body and other tumors of the neck not only as far as an accurate preoperative diagnosis is concerned but also from the standpoint of operative management.

Carotid body tumors are not common, and only about 350 have been recorded in the literature. Only 10 were seen in a nine-year period on the head and neck service of the Memorial Hospital, where 1200 new patients are seen yearly. At Passavant Memorial Hospital only two carotid body tumors have been encountered in some 25 years.

Probably because of their relative rarity, the correct preoperative diagnosis of a carotid body tumor is not often made, and its intimate relationship to the carotid vessels is only discovered upon surgical exposure. In Lahey's series of 18 patients, the correct preoperative diagnosis was made in only 9.[1] The reports of other series contain an almost equal number of mistaken diagnoses.[2-4] These tumors may be mistaken for aneurysms of the carotid arteries, aberrant thyroid tissue, lymphadenopathy, or branchial cysts. Because of their frequent pulsatile character, they are often mistaken for aneurysms. Their consistency to palpation is reported to vary considerably, from the firmness of the so-called potato tumor to the soft, compressible type which may be almost obliterated by carotid compression.[2] More than one of the latter type has probably been treated by proximal ligation on the assumption that the mass was an aneurysm.[2]

Insofar as the surgical management of carotid body tumors is concerned, there is considerable difference of opinion. Certainly there is some question as to whether these are benign or malignant tumors. Biopsy of such a tumor does not always answer this question, since the histological appearance and clinical behavior of these tumors may not be similar. LeCompte[5] has stressed this point and, as a pathologist, believes that these tumors should not be operated upon, considering what he feels is an inordinate surgical morbidity and mortality should carotid ligation be necessary. Biopsy of such a vascular tumor may not always be feasible, especially if the tumor proves too late to be an aneurysm.

Of great importance is the relationship of carotid body tumors to the vessels themselves in the plan of surgical management. To be forewarned is to be forearmed. It is better to be prepared to spend the time

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necessary to excise such a tumor without damaging the vessels, or, should ligation be necessary, to know of the adequacy of collateral cerebral circulation. Further, it would appear desirable, should resection of the carotid be inevitable, to have available whatever might seem necessary for a blood vessel replacement or anastomosis. The feasibility of such grafting or anastomosis, for example, between the internal carotid, superiorly, and the external carotid, inferiorly, would depend largely on the superior extent of the tumor and the amount of extracranial internal carotid artery available. It is our opinion that the presence or absence of hemiparesis following carotid ligation may be strongly influenced by the general state of the patient at the time of ligation, but even more by the type of anesthetic used. In our series of 108 carotid ligations for intracranial vascular disease, most of the hemiplegias occurred after ligation in the anesthetized patient who was in shock.[6] The percentage of patients who are hemiplegic after carotid ligations done during radical neck dissections for head and neck tumors[7] is many times that which is found in series of carotid ligations done for intracranial aneurysms. It may well be that the two factors of general anesthesia and blood loss may account for these differences. Ralston, Rasmussen, and Kennedy[8] have shown that the extent of cerebral infarction following middle cerebral artery occlusion in the monkey varies considerably and is dependent upon the blood pressure at the time of occlusion, and is much greater in animals hypotensive from blood loss than in those rendered hypotensive by ganglionic blocking agents.

The first of our patients was a 53-year-old housewife who had for several years complained of a pulsatile mass below the angle of the jaw on the left. She was thought by her physician and several others to have an aneurysm of the carotid artery. The mass had gradually been increasing in size. It was relatively firm in consistency but with compression could be somewhat reduced in size. An easily audible bruit could be heard on auscultation. It was movable in the horizontal plane but not in the vertical plane. It measured about 5×5×7 cm.

Fig. 1.—Carotid angiogram, showing carotid body tumor.

A carotid arteriogram was done under local anesthesia without difficulty and the carotid system visualized in both its intra and its extracranial portion (Fig. 1). The tumor mass was situated at the carotid bifurcation and appeared to be well vascularized. Good flow of the contrast medium across the anterior communicating artery was also demonstrated.

The patient was operated on under local anesthesia and with an adequate incision extending from the tip of the mastoid to just above the clavicle along the anterior border of the sternocleidomastoid muscle. The common carotid artery was exposed and a piece of rubber drain placed about it which could be used to occlude the vessel as desired. The tumor and the carotid vessels above were then exposed. An attempt was made to dissect out the internal carotid artery, but this was not entirely successful because the vessel tore in the region of the carotid bulb. The common carotid, the internal carotid above the tumor, and the external carotid above the bulb were then ligated and the mass removed. The postoperative course was uneventful, without any evidence of paralysis.

The next patient was a 67-year-old woman with a similarly placed mass which was also pulsatile and which was also increasing in size. A bruit could be easily heard on auscultation. Carotid angiography was done to determine the exact nature of the mass, although an aneurysm was suspected. The films revealed a large aneurysm of

Fig. 2.—Carotid angiogram, showing aneurysm of cervical portion of internal carotid artery.

the internal carotid artery (Fig. 2), which was treated by simple common carotid ligation and subsequent improvement, without paralysis.

Comment

Carotid angiography has seldom been used as a diagnostic aid in the treatment of tumors of the neck. Only a few instances have been reported of its use in carotid body tumors.[9,10] It would appear to us that this relatively safe procedure is of considerable value, particularly insofar as tumors of the upper portion of the neck are concerned, because one may demonstrate the relationship of the tumor mass and the carotid vessels. This is of value both for diagnosis and for subsequent therapy. The angiographic appearance of a carotid body tumor is quite characteristic, as is that of aneurysms. The identification of vessels is not difficult if films in the anteroposterior and lateral projections are obtained. Percutaneous angiography is not difficult and is relatively safe.

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REFERENCES

1. Lahey, F. H., and Warren, K. W.: Long Term Appraisal of Carotid Body Tumors with Remarks on Their Removal, Surg. Gynec. & Obst. 92:481-491, 1951.

2. Monro, R. S.: Natural History of Carotid Body Tumours and Their Diagnosis and Treatment, with a Report of 5 Cases, Brit. J. Surg. 37:445-453, 1950.

3. Gratiot, J. H.: Carotid-Body Tumors: Collective Review, Internat. Abstr. Surg. 77:177-186, 1943, in Surg. Gynec. & Obst., Sept., 1943.

4. Harrington, S. W.; Clagett, O. T., and Dockerty, M. B.: Tumors of the Carotid Body: Clinical and Pathologic Considerations of Twenty Tumors Affecting Nineteen Patients (One Bilateral), Ann. Surg. 114:820-833, 1941.

5. LeCompte, P. M.: Tumors of the Carotid Body and Related Structures (Chemoreceptor System), in Atlas of Tumor Pathology, published by U. S. Armed Forces Institute of Pathology, Washington, D. C., Sect. IV, Fasc. 16, 1951.

6. Davis, R. A.; Wetzel, N., and Davis, L.: Analysis of the Results of Treatment of Intracranial Vascular Lesions by Carotid Artery Ligation, Ann. Surg. 143:641-650, 1956.

7. Moore, O., and Baker, H. W.: Carotid-Artery Ligation in Surgery of the Head and Neck, Cancer 8:712-726, 1955.

8. Ralston, B.; Rasmussen, T., and Kennedy, T.: Occlusion of the Middle Cerebral Artery Under Normotension, and Anemically Induced and Chemically Induced Hypotension, J. Neurosurg. 12:26-33, 1955.

9. Idbohrn, H.: Angiographical Diagnosis of Carotid Body Tumours, Acta radiol. 35:115-123, 1951.

10. Lichtenauer, F.: Operationsindikation und Arteriographie bei Carotisdrüsengeschwülsten, Zentralbl. Chir. 41:2286-2287, 1938.

DISCUSSION

ON PAPERS BY DRS. SZILAGYI, WHITCOMB, AND SHONNARD AND DR. WETZEL

DR. LOUIS G. HERRMANN, Cincinnati: I must apologize for coming to the rostrum so soon again, but I cannot allow this excellent presentation by Dr. Szilagyi and his group to pass without a few comments.

Dr. Szilagyi and Dr. Whitcomb have presented a most interesting study on the replacement of peripheral arteries by the use of permeable plastic tubes. We also have been interested in the various

means of promoting arteriogenesis in man. From the data which have just been presented, there should be little doubt in your minds that arteriogenesis offers a logical and practical means of bridging long defects in peripheral arteries of small caliber.

Homologous and heterologous grafts of blood vessels have been studied for more than 50 years, but, until we learn more about the mechanism by which the human body will accept or reject tissue from other sources, we shall not have solved our problem.

I wish to commend the authors on their excellent work. We are convinced that arteriogenesis is a logical means of creating new arterial pathways in human extremities.

DR. JOHN H. OLWIN, Chicago: I should like to congratulate Dr. Szilagyi and his group on this very fine addition to the problem of substitution grafts.

The big problem we have, particularly in the femoral area, is the obtaining of satisfactory lengths of homografts, and up to the present time the various synthetic substitutions have not been satisfactory.

We feel that the best thing to use here, where it is available, is an autogenous substance, and up to the present time the saphenous vein is the only thing we have available. Unfortunately, autogenous grafts are not always available in the patients who need them. Homogenous grafts have been used with some benefit, but it seems to me that the authors' graft, as far as the prosthetic type is concerned, is probably the best we have at this time. It will certainly be some years before we have any real information as to what is the best type of graft. We have been trying to build up as large a series of autografts as possible for purposes of their proper evaluation. We have been reasonably satisfied with the ones we have been able to place.

Dr. Szilagyi is pioneering in this field, and I should like again to congratulate him and his group on this very fine addition to our present knowledge.

DR. D. EMERICK SZILAGYI, Detroit: Dr. Whitcomb and I should like to thank Dr. Herrmann and Dr. Olwin for their pertinent and kind remarks. I should also like to make one or two points, very briefly.

As you well know, the principal motivation of the search for plastic substitutes has been the great practical advantage of the easy availability of these prostheses. But recently the urgency of the need for implants of this type has been intensified by another factor, namely, the realization that on longer follow-up—say two to three years after operation—an alarming percentage of homografts are found to have undergone degenerative changes. There is good reason to believe that this late deterioration would not take place in certain types of plastic prostheses.

The prosthesis we presented has some very nice qualities, but one must not overlook its shortcomings, most of which are minor, but one of which, namely, the loss of tensile strength after implantation, deserves special emphasis. In fact, in purely numerical terms, this loss of tensile strength is quite alarming. A consideration of the meaning of the numerical factors involved, however, shows that the drop in tensile strength is not as dangerous as it first appears. This analysis of the factors is given in detail in the manuscript version of the paper. Briefly stated, the tensile strength of the nylon fabric, even after its observed reduction, is not significantly below that of the normal dog aorta, and is above what can be regarded as the minimum of safety. This conclusion is in keeping with the observed lack of any changes in the implants up to 12 months that would suggest dangerous loss of the integrity of the wall. An added factor of safety is the circumstance that after 10 months only one-third of the tensile strength of the implants depends on the integrity of the fabric.

We are undertaking experiments with the view to improving the tensile quality of the prosthesis. In the meantime, the potential danger of the loss of tensile strength must be kept in mind. With respect to clinical application, it definitely would not appear safe to use the prosthesis in the aortic area.

DR. JOHN G. WHITCOMB, Detroit: I would like to thank the association for the opportunity of presenting this paper at this meeting.

DR. WALTER WILLIAM CARROLL, Chicago: I should like to congratulate Dr. Wetzel on this very interesting presentation. There is no doubt that this idea is a clever one, even though the application may be somewhat limited. There are occasional instances in neoplastic head and neck surgery in which one is seriously concerned about the integrity of the carotid artery.

It is true that one can make the justifiably critical observation that in the great majority of such instances excisional surgery may offer little in the way of long-term salvage.

On the other hand, in the case of slow-growing tumors and certain radiation failures, experience will show that one can justifiably defend a generous surgical effort. In such circumstances it is interesting to note how one's attention becomes fixed upon the carotid artery. It soon becomes evident that one's aggressiveness is tempered by reverence for this vessel. I should like to show a slide to exemplify this.

[Slide] This is a photograph showing a rather extensive tumor that has recurred after radiation.

It arose from the gingiva and grew not only superficially, through the skin, but deep, and definitely altered the relationships of the carotid artery.

It was our feeling that this tumor might be categorically inoperable. Certainly, the disease was far advanced. We asked Dr. Wetzel to do a carotid angiogram on this patient. He obtained an excellent view, showing that the carotid artery was simply displaced, but there was no marked alteration of the wall of the artery.

[Slide] The next slide shows the deep extension of this kind of tumor, as you see here, where it encroached on the carotid artery. We were able to remove this tumor, since it peeled off without any difficulty.

It seems to me that in the past we have not availed ourselves of all the possible diagnostic help prior to such surgery or prior to a decision against surgery in such extensive tumors.

If carotid angiograms are used more frequently, the resultant radiographic findings might very well be indicative of facile operability, or perhaps indicate obvious carotid arterial wall involvement. In either event, the information can be helpful to the surgeon.

Evaluation of Venous Shunt Surgery in Portal Hypertension

WILLIAM S. DYE, M.D.; RICHARD B. CAPPS, M.D.; LYLE A. BAKER, M.D.; WILLIAM J. GROVE, M.D., and ORMAND C. JULIAN, M.D., Chicago

The surgical treatment of portal hypertension has depended primarily on the use of portacaval or splenorenal shunts.[1-13] The shunt procedures are usually performed in patients who have hemorrhaged from esophageal varices, the surgery being done during a quiescent period. The use of balloon tamponade has been the most universal method of controlling the acute bleeding from esophageal varices.[14] Recently, however, portacaval shunts have been recommended as an emergency procedure in acutely bleeding patients.[15] Difficulty in the management of these patients, particularly the cirrhotic patient, has led to the introduction of various other procedures, such as gastroesophageal reaction,[16,17] transection of the upper stomach with resuturing,[18,19] and transesophageal ligation of varices.[20-22] Ligation of arterial supply to the liver and spleen has also been advocated by some.[23-26] Much of the difficulty in comparing mortality of surgically and medically treated patients is the great influence exerted on surgical mortality of the criteria of operability in any series.

Selection of Patients

Patients selected for venous shunt surgery have been limited in this series to those who have had upper gastrointestinal hemorrhage from esophageal varices. No prophylactic shunts have been performed on patients with esophageal varices who have not bled. Patients with poor liver function and who are, therefore, poor risks, have been included for surgery. Such patients have shown albumin levels below 3.0 gm. per 100 cc., sulfobromophthalein (BSP) retention above 25%, and elevated serum bilirubin, as well as other evidences of severe liver dysfunction. These are the patients, as Blakemore has pointed out, that carry a higher surgical mortality. Approximately 50% of the patients operated on fell into this group. A period of medical therapy varying from two or three weeks to several months from time of hemorrhage has been instituted in each case prior to surgery.

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Material and Technique

A total of 79 venous shunt operations were performed. Included are 47 splenorenal anastomoses and 22 portacaval shunts. In eight other patients multiple procedures were necessary (Table 1).

TABLE 1.—*Summary of Venous Shunts*

Type of Procedure	No. of Cases
Splenorenal	47
Portacaval	22
Multiple procedures	8

The etiology of the portal hypertension is summarized in Table 2. Of the 47 patients having a splenorenal shunt, 24 were classified as poor risks. Eight cases not included in this report were explored but no shunt was performed. These latter cases were thought to represent regression of portal hypertension on medical management.[27,28]

TABLE 2.—*Cause of Obstruction*

Laennec's cirrhosis	53
Postnecrotic	4
Biliary cirrhosis	1
Hepatoma	1
Extrahepatic	10

The diagnosis of intra- or extrahepatic obstruction has been made in the majority of cases on a clinical basis. Recently we have turned to the use of splenoportography as an aid in defining the point of obstruction (Figure).

The technique of portacaval and splenorenal shunts has been described in detail elsewhere.[29,30] We have used a thoracoabdominal approach through the 8th or 9th interspace on the right for portacaval shunts and through the 10th or

Splenoportagram in patient with intrahepatic portal obstruction due to Lannec's cirrhosis. Visualization was accomplished by direct puncture of the spleen, using 35% iodopyracet (Diodrast).

11th interspace on the left for splenorenal shunts. A right subcostal abdominal incision has been used in a few thin patients and has been satisfactory for portacaval anastomoses. Portacaval shunts are technically easier than splenorenal anastomoses because of the thicker wall of the portal vein and the greater ease of dissection. Both anastomoses have been done in the end-to-side manner, using a simple continuous over-and-over suture in most cases. Heparin has not been used either during or after surgery.

Results

The results in 47 cases having a splenorenal shunt are summarized in Table 3. A total of 26 patients have survived, with a follow-up period of six months to eight years, 11 patients having been followed more than five years. Of the total 47 cases, 24 were poor-risk patients. Of these, 10 are among the 26 surviving patients, 2 having been followed more than five years and 8 less than five years. The operative mortality is 25.3%.

TABLE 3.—*Splenorenal Shunts*

Postoperative deaths	12
Late deaths	9
Alive (6 mo.-8 yr.)	26
(11 cases followed over 5 yr.)	
Total	47

TABLE 4.—*Portacaval Shunts*

Postoperative deaths	4
Late deaths	4
Alive (6 mo.-8 yr.)	14
(2 followed over 5 yr.)	
Total	22

A summary of the portacaval shunts is shown in Table 4. Fourteen patients have survived, with a follow-up period of six months to eight years, two patients being followed over five years. Of the total of 22 cases, 11 were poor-risk patients. Five of these are among the fourteen surviving patients. The operative mortality is 18.1%.

The results in eight additional patients requiring multiple procedures are summarized in Table 5. Five of these eight patients had had splenectomies elsewhere. One notes that as many as three or four different procedures have been done on some patients. Four of the eight patients requiring multiple procedures had good results. One is dead, and three have had recurrence of bleeding. Case 3 is of interest. At 10 years of age

TABLE 5.—*Multiple Procedures*

Case	Splenectomy	Splenorenal Shunts	Portacaval Shunts	Resection Lower Esophagus	Mesenteric-Cavel Shunt	Ligation Varices	Results
1	+			+	+		Good
2	+					+	Varices remain
3	+	+		+	+		Bleeding recurred
4		+				+	Good
5		+	+				Bleeding recurred
6	+	+					Good
7		+	+	+			Good
8	+	+					Good

TABLE 6.—*Postshunt Bleeding*

	Living Patients	Deaths	Total	Cases	%
Portacaval	4	4	8	22	36
Splenorenal	5	5	10	47	21

a splenectomy was performed, followed within the next four years by splenorenal shunt using a remnant of a splenic vein, resection of the lower esophagus, and superior mesenteric-caval shunt. This patient has bled after each procedure but is still alive. Case 7 is of interest because both a splenorenal and a portacaval anastomosis, as well as resection of the esophagus, were done. In spite of these procedures, varices persisted above the line of anastomosis of the esophagus to the stomach. The patient subsequently died of hemorrhage.

The incidence of postshunt bleeding is summarized in Table 6. Postshunt bleeding has occurred in four living patients who have had a portacaval shunt and in five having a splenorenal shunt. Four patients having a portacaval shunt and five having a splenorenal shunt had gastrointestinal hemorrhage as a contributing cause to their death. It is impossible to say whether this hemorrhage is actually due to bleeding esophageal varices, terminal hypoprothrombinemia, or other causes. These are included, however, giving an over-all incidence of 36% postshunt bleeding in portacaval shunts and 21% in splenorenal shunts.

Two patients having a portacaval shunt have shown persistence of a preexisting hypersplenism. Both exhibited anemia, leukopenia, and thrombocytopenia following surgery. The failure of hypersplenism to respond to portal decompression by portacaval anastomosis has previously been reported by Macpherson.[31]

Comment

The results reported represent a series of patients all of whom have had bleeding from esophageal varices and in whom venous shunts have been constructed to reduce the portal pressure. In recent years the choice of procedure has tended toward the use of a portacaval shunt. One can say from this experience that technically a better shunt may be constructed with a portacaval anastomosis. Although operative mortality appears less with portacaval anastomosis than with splenorenal anastomosis, we do not feel the difference is significant, since the cases are difficult to compare. Others have reported a greater mortality following portacaval anastomosis.

The effects of shunting all the portal blood flow away from the liver, as in a portacaval shunt, have not as yet been clearly defined. There is indication that there is an advantage in doing splenorenal shunts in patients with splenomegaly and hypersplenism. Reinforcement for this view will be gained if further cases of persistent hypersplenism following portacaval shunts are reported.

Although establishment of shunts between the portal and the systemic vein offers the only real means of reducing portal hypertension, evaluation of these procedures still presents a problem. In particular, the management of the cirrhotic patient with bleeding esophageal varices is difficult because of the many variables which affect his survival, whether or not he is operated upon. Snell's[32] studies have indicated the high mortality in bleeding esophageal varices when medically treated. Macpherson has shown only a slight improvement in the survival rate of patients having a venous shunt operation as compared with patients treated medically. There is further need for a large, carefully followed series using medical management alone.

Blakemore[12] and Linton[6] have shown a good salvage rate with portacaval and splenorenal shunts. Recently Linton has employed transesophageal ligation of varices in the massively bleeding patient in order to tide him over for future shunt surgery.[22]

It has been shown by us and by others that varices do recede on medical management. Such recession of varices is particularly apparent in the patient with an acute fatty liver following excessive alcoholic

intake. The question is raised, therefore, of the validity of prophylactic shunts, as reported by Brick and Palmer.[34] At the present time we do not feel justified in subjecting patients to surgery who have never bled.

In the series presented, poor-risk patients have been included. Approximately 50% of the patients presenting themselves fall into this category. Including these patients raises the surgical mortality and over-all survival. The question arises as to whether one is justified in operating upon poor-risk patients.

Finally, there seems to be little doubt that abstinence from alcohol is the most important factor in the management of the cirrhotic patient, whether or not he is surgically treated. It is believed that many of the poor results in surgically treated patients are due to continued drinking.

Summary

Experience with venous shunts for portal hypertension is presented. Sixty-nine patients were subjected to a shunt procedure as the single method of surgical treatment, 47 having a splenorenal and 22 a portacaval shunt. Eight additional patients had multiple procedures performed.

The over-all operative mortality was 25.3% in splenorenal and 18.1% in portacaval shunts. Of the 47 patients having a splenorenal shunt, 26 have survived during a six-month to eight-year follow-up. Of the 22 patients having a portacaval shunt, 14 survived during a similar follow-up.

Postshunt bleeding has occurred in 36% of patients having a portacaval shunt and in 21% having a splenorenal shunt. Both the living patients and those who may have had bleeding as a part of their terminal illness are included.

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REFERENCES

1. Whipple, A. O.: Problem of Portal Hypertension in Relation to the Hepatosplenopathies, Ann. Surg. 122:449-475, 1945.

2. Blakemore, A. H., and Lord, J. W., Jr.: Technic of Using Vitallium Tubes in Establishing Portacaval Shunts for Portal Hypertension, Ann. Surg. 122:476-489, 1945.

3. Blalock, A.: Use of Shunt or By-Pass Operations in Treatment of Certain Circulatory Disorders, Including Portal Hypertension and Pulmonic Stenosis, Ann. Surg. 125:129-141, 1947.

4. Blakemore, A. H.: Indications for Portacaval Anastomosis: Analysis of Cases, Surg. Gynec. & Obst. 84:645-653, 1947.

5. Blakemore, A. H.: Portacaval Anastomosis, Surg. Gynec. & Obst. 87:277-279, 1948.

6. Linton, R. R.; Hardy, I. B., Jr., and Volwiler, W.: Portacaval Shunts in Treatment of Portal Hypertension: Analysis of 15 Cases with Special Reference to Suture Type of End-to-Side Splenorenal Anastomosis with Splenectomy and Preservation of Kidney, Surg. Gynec. & Obst. 87:129-144, 1948.

7. Linton, R. R.: Surgical Treatment of Bleeding Esophageal Varices by Portal-Systemic Venous Shunts, with Report of 34 Cases, Ann. Int. Med. 31:794-804, 1949.

8. Julian, O. C.: Choice of Operation in Portal Hypertension with Varices, Surg. Gynec. & Obst. 100:753-754, 1955.

9. Hughes, C. W., and Jahnke, E. J.: Surgical Aspects of Portal Decompression, Am. J. Gastroenterol. 24:372-377, 1955.

10. Julian, O. C., and Dye, W. S.: Venous Shunts in Portal Hypertension, A. M. A. Arch. Surg. 63:373-378, 1951.

11. Learmonth, J.: On Certain Aspects of Portal Hypertension, Edinburgh M. J. 58:1-16, 1951.

12. Blakemore, A. H.: Portacaval Shunting for Portal Hypertension, Surg. Gynec. & Obst. 94: 443-454, 1952.

13. Altemeier, W. A.; Hoxworth, P. I.; McElhinney, W. T.; Giuseffi, J.; Mac Millan, B., and Todd, G.: Treatment of Portal Hypertension, Am. Surgeon 20:1235-1245, 1954.

14. Sengstaken, R. W., and Blakemore, A. H.: Balloon Tamponage for the Control of Hemorrhage from Esophageal Varices, Ann. Surg. 131: 781-789, 1950.

15. O'Sullivan, W. D., and Payne, M. A.: Emergency Portacaval Shunt, Surg. Gynec. & Obst. 102:668-676, 1956.

16. Phemister, D. B., and Humphreys, E. M.: Gastro-Esophageal Resection and Total Gastrectomy in Treatment of Bleeding Varicose Veins in Banti's Syndrome, Ann. Surg. 126:397-410, 1947.

17. Cooley, D. A., and DeBakey, M. E.: Subtotal Esophagectomy for Bleeding Esophageal Varices, A. M. A. Arch. Surg. 68:854-871, 1954.

18. Tanner, N. C., in Discussion: Gastroduodenal Hæmorrhage as a Surgical Emergency, Proc. Roy. Soc. Med. 43:147-152, 1950.

19. Allen, J. G., and Head, L. R.: Diagnosis of Portal Hypertension with Notes on Treatment, S. Clin. North America 36:119-130, 1956.

20. Boerema, I., cited by Hunt, A. H.: Discussion on Portal Hypertension, Proc. Roy. Soc. Med. 47:19, 1954.

21. Crile, G., Jr.: Transesophageal Ligation of Bleeding Esophageal Varices: Preliminary Report of 7 Cases, Arch. Surg. 61:654-660, 1950.

22. Linton, R. R., and Ellis, D. S.: Emergency and Definitive Treatment of Bleeding Esophageal Varices, J. A. M. A. 160:1017-1023, 1956.

23. Rienhoff, W. F., Jr.: Ligation of the Hepatic and Splenic Arteries in the Treatment of Portal Hypertension with a Report of 6 Cases: Preliminary Report, Bull. Johns Hopkins Hosp. 88:368-375, 1951.

24. Berman, J. K.; Koenig, H., and Muller, L. P.: Ligation of Hepatic and Splenic Arteries in Treatment of Portal Hypertension, A. M. A. Arch. Surg. 63:379-389, 1951.

25. Blain, A. W., and Blain, A., III: Ligation of Splenic Artery, Operation of Choice in Selected Cases of Portal Hypertension and Banti's Syndrome, Ann. Surg. 131:92-99, 1950.

26. Everson, T. C., and Cole, W. H.: Ligation of Splenic Artery in Patients with Portal Hypertension, Arch. Surg. 56:153-160, 1948.

27. Dye, W. G.; Bennett, H. D.; Baker, L., and Julian, O.: Observations on the Inconstancy of Portal Hypertension in Hepatic Cirrhosis, S. Forum, 3:496, 1952.

28. Bennett, H. D.; Lorentzen, C., and Baker, L. A.: Transient Esophageal Varices in Hepatic Cirrhosis, A. M. A. Arch. Int. Med. 92:507-522, 1953.

29. Satinsky, V. P.: Portacaval Shunt for Portal Hypertension: A New Approach, Editorial, Rev. Gastroenterol. 15:333-334, 1948.

30. Hallenbeck, G. A.: Portacaval Anastomosis: Rationale, Indications and Technique, S. Clin. North America 35:1099-1115, 1955.

31. Macpherson, A. I. S.: Some Problems Involved in the Treatment of Portal Hypertension, Edinburgh M. J. 60:13-27, 1953.

32. Snell, A. M.: Discussion of Symposium on Hepatic Circulation, Proc. Staff Meet. Mayo Clin. 25:36-38, 1950.

33. Macpherson, A. I. S.; Owen, J. A., and Innes, J.: Surgical Treatment of Portal Hypertension: Results in 64 Cases, Lancet 1:353-357, 1956.

34. Brick, I. B., and Palmer, E. D.: Management of Esophageal Varices in Cirrhosis of the Liver in the Absence of Gastrointestnial Hemorrhage, South. M. J. 48:1021-1023, 1955.

Studies of Hepatic Function in Dogs with Eck Fistula or Portacaval Transposition

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There is considerable evidence that impairment of hepatic function occurs when the hepatic blood flow is reduced. Whipple[1] and Knutti[2] have shown that production of hemoglobin and serum proteins in animals with an Eck fistula is below normal. Harper et al.[3] have found decreased tolerance to orally administered amino acids in dogs with Eck fistulas. Several authors have found clinical evidence of progressive deterioration of hepatic function following surgically constructed portacaval shunts.[4,5] Reduction of hepatic blood flow has also resulted in impairment of regeneration of liver tissue. Mann and Magath[6] have shown that there is an almost complete disappearance of the regenerative capacity of the liver following the production of an Eck fistula. On the other hand, the liver will regenerate very well when a portacaval transposition has been carried out, indicating that portal blood per se is unnecessary for regeneration of the liver.[7]

The deterioration of liver function that follows the production of an Eck fistula in dogs may be ascribed either to diversion of the portal blood from the liver or to the reduction in the supply of blood that results from this operation. The following experiments were carried out to study the relative importance of these factors.

Method

A total of 12 adult mongrel dogs were operated upon for this study. All surgical procedures were carried out with intravenous pentobarbital (Nembutal) sodium anesthesia and aseptic precautions. In six dogs (Group 1) an Eck fistula was produced through a right thoracoabdominal incision, by means of a side-to-side portacaval anastomosis, with ligation and division of the portal vein above this anastomosis. Six dogs (Group 2) underwent the operation of transposition of the portal vein and vena cava, which was carried out in the manner described by Child[7] (Fig. 1). In both groups,

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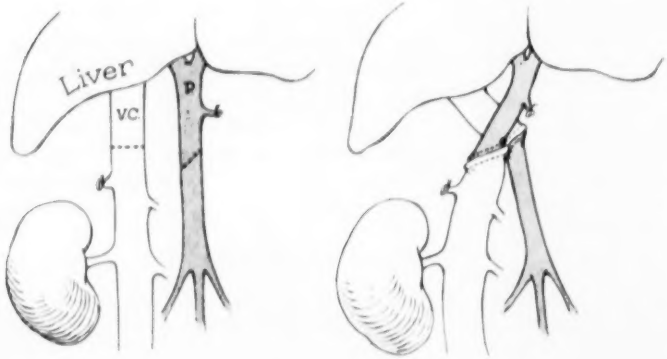


Fig. 1.—Diagram of the method used to transpose the portal vein and vena cava in a dog.

all tributaries of the portal vein above its anastomosis with the vena cava were divided and ligated, in order to destroy as completely as possible the portal blood supply to the liver. In the animals undergoing portacaval transposition the right adrenal vein was ligated in some cases when necessary to obtain sufficient length for anastomosis. All animals were given 300,000 units of penicillin daily for five days following operation.

The laboratory studies described below were carried out preoperatively and at intervals of one week, one month, two months, and three months after operation. Complete studies were accomplished in nine dogs.

Total protein, albumin, and globulin determinations were done by the biuret method,[8] and thymol turbidity was studied by the method of Maclagan[9] as modified by Mateer.[10] The clearance of sulfobromophthalein (Bromsulphalein) was determined by the method of Goodman[11] as follows: Five milligrams of sulfobromophthalein per kilogram of body weight was injected into a vein of the foreleg of the fasting animals. Specimens of blood were taken at intervals of 5 minutes for 20 minutes following injection, the intervals being timed with a stop watch. The sulfobromophthalein content of the blood was measured according to the method of Gaebler.[12] In the calculation of the clearance of sulfobromophthalein, the plasma volume of each animal was computed by extrapolation of the sulfobromophthalein concentrations to zero time; the plasma volumes so obtained, together with the measured serum albumin concentrations, were used to compute the total circulating albumin.

Tolerance to orally administered ammonium lactate was determined in the following manner: After samples of blood had been taken from animals while in the fasting state for an estimation of the level of ammonia nitrogen a test dose of 0.33 gm. of ammonium lactate per kilogram of body weight was given to all animals prior to operation, as well as to those animals in Group 2 (with portacaval transposition); because preliminary studies had shown that these dogs tolerated the larger test dose very poorly, one-half that dose was administered in the same way to the animals with Eck fistulas. In the animals not operated on specimens of blood were drawn at 15, 30, 60, and 90 minutes following the test dose of ammonium lactate. In all the tests following operation, specimens of blood were taken at 30, 60, 120, and 180 minutes after the dose of the ammonium salt. The ammonia nitrogen content of each sample of blood was promptly determined, using a modification of the microdiffusion method of Conway.[13]

The body weight of each animal in the fasting state was recorded at the time of each of the laboratory tests. The dogs were killed at the end of these studies, and examination of either the Eck fistula or of the two anastomoses of the portacaval transposition was made to determine their patency. The livers were weighed immediately in the fresh state, after as much as possible of the blood had been allowed to drain from them. Specimens of one of the kidneys and of three different lobes of the liver were obtained for microscopic examination. In addition to the usual stains, special glycogen (Schiff's) and fat (oil red O) stains were used to study the liver specimens.

Results

All of the dogs survived the test period. The vascular anastomoses between the portal vein and the vena cava were found to be patent in all of the animals, with one exception.

TABLE 1.—*Changes in Body Weight of Dogs with Eck Fistula*

Dog No.	Preoperative Weight, Kg.	Weight 3 Mo. Postoperative, Kg.
62	14.0	12.7
22	16.8	15.2
19	16.2	13.5
143	12.9	10.0
186*	16.5	13.3
Mean loss in body weight 2.34 kg.		

* Dog that had a portacaval transposition with thrombosis of the anastomosis between the distal vena cava and the proximal portal vein.

The total circulating plasma albumin decreased in every dog with an Eck fistula, with a mean loss of 19.9 gm. (Table 1). On the other hand, with one exception, the total circulating albumin increased in all animals with a transposition of the portal vein and vena cava (Table 2). The mean gain for this group, including the loss sustained by one animal, was 13.8 gm. over a three-month period. The globulin fractions of the plasma were not significantly altered in either group of dogs. The results of the thymol turbidity test remained normal in all of the animals.

TABLE 2.—*Changes in Body Weight of Dogs with Portacaval Transposition*

Dog No.	Preoperative Weight, Kg.	Weight 3 Mo. Postoperative, Kg.
138	12.0	11.4
154	9.3	16.0
113	13.5	12.7
168	14.3	15.3
157	15.0	14.6
Mean loss in body weight 0.1 kg.		

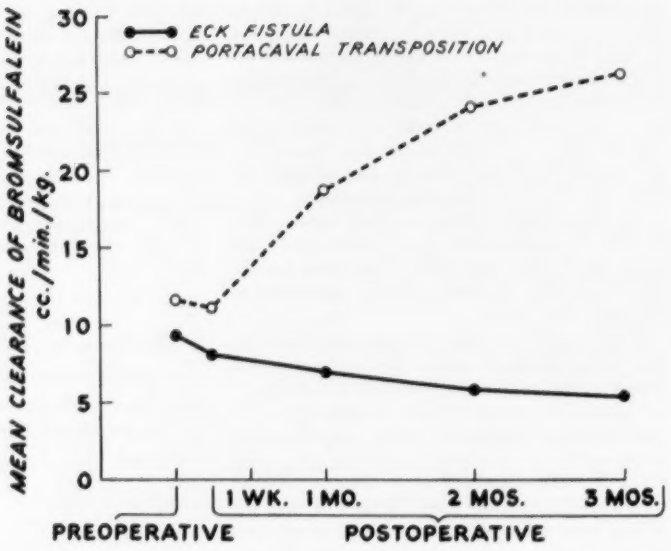


Fig. 2.—Mean values for sulfobromophthalein (Bromsulfalein) clearance of animals with Eck fistulas or portacaval transpositions preoperatively and at intervals of one week, and one, two, and three months after operation.

The clearance of sulfobromophthalein decreased in every animal with an Eck fistula but rose markedly in every dog with a portacaval transposition. Figure 2 shows the mean values for sulfobromophthalein clearance for both groups of animals at each test interval. A decline in sulfobromophthalein clearance immediately after the production of a portacaval anastomosis would be expected to occur merely as a result of the decrease in the blood supply to the liver which follows this procedure.[14] However, the continuing and progressive decrease in the clearance of sulfobromophthalein that occurred in the dogs with Eck fistulas indicated that additional factors were responsible. This may be ascribed either to further reduction in blood flow or to intrinsic deterioration of hepatic function or to both. It is probable that a depression of the hepatic function is the causative factor, because it is known that collateral circulation to the liver tends to increase rather than decrease following interruption of the portal vein.

Figure 3 shows that in both groups of dogs tolerance to orally administered ammonium lactate was diminished after operation. This was much more evident, however, in the dogs with Eck fistulas. The mean values for the peak levels of ammonia nitrogen attained in the tolerance tests were 4.56γ and 3.97γ per milliliter for Groups 1 and 2, respectively, despite the fact that the dogs with the Eck fistulas (Group 1) received only one-half the dose of ammonium lactate given to the other animals. However, the rate of disappearance of ammonium nitrogen from the blood, as judged by the levels of blood ammonia nitrogen observed at subsequent intervals, was not significantly different in the two groups of animals.

Figure 4 illustrates that the mean fasting level of ammonia nitrogen in the blood of all these dogs increased within three months after operation. The increase was slight in the animals with portacaval transposition but reached abnormally high levels in the group with Eck fistulas.

There was a rather marked difference in the general condition of the two groups of dogs as the experiment progressed. All of the animals with Eck fistulas lost weight and had a tendency to anorexia, lassitude, and polydipsia. The mean weight loss of the dogs with an Eck fistula was 2.34 kg. over a three-month period, whereas the

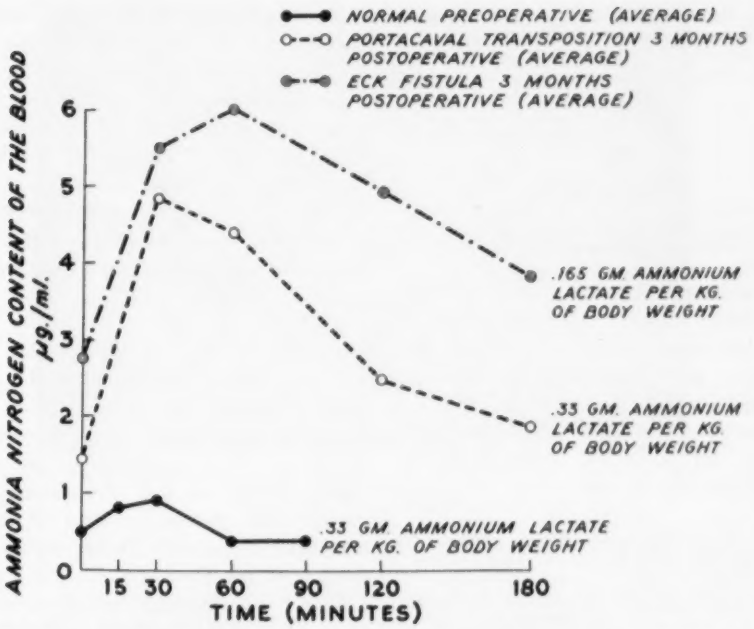

NORMAL PREOPERATIVE (AVERAGE)
PORTACAVAL TRANSPOSITION 3 MONTHS POSTOPERATIVE (AVERAGE)
ECK FISTULA 3 MONTHS POSTOPERATIVE (AVERAGE)
AMMONIA NITROGEN CONTENT OF THE BLOOD μg./ml.
.165 GM. AMMONIUM LACTATE PER KG. OF BODY WEIGHT
.33 GM. AMMONIUM LACTATE PER KG. OF BODY WEIGHT
.33 GM. AMMONIUM LACTATE PER KG. OF BODY WEIGHT
0
1
2
3
4
5
6
15 30 60 90 120 180
TIME (MINUTES)

Fig. 3.—Ammonia nitrogen content of the blood in normal dogs, dogs with Eck fistulas, and dogs with portacaval transpositions after oral administration of a dose of ammonium lactate.

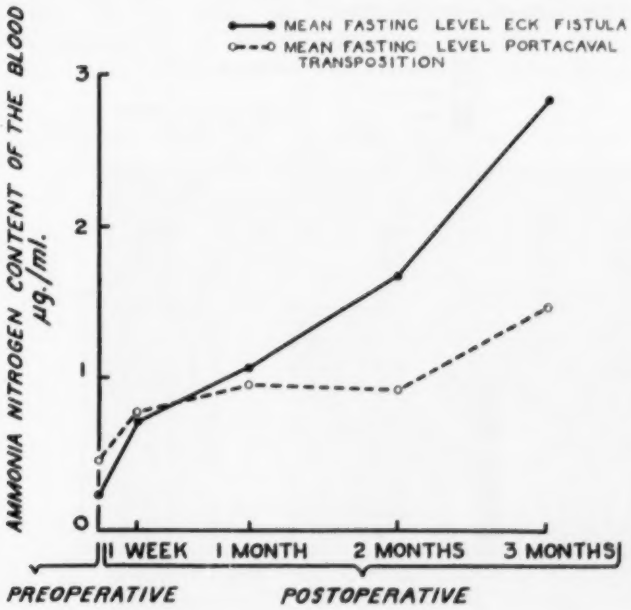


Fig. 4.—Mean fasting levels of ammonia nitrogen in the blood of dogs with Eck fistulas or portacaval transpositions preoperatively and at various intervals postoperatively.

TABLE 3.—*Total Circulating Plasma Albumin, in Grams, in Dogs with Eck Fistula*

Dog No.	Preoperative	Three Mo. Postoperative	Net Change
62	39.7	19.6	−20.0
22	70.7	33.6	−37.1
143	19.3	17.3	− 2.0
19	52.0	21.4	−30.6
156*	40.0	30.1	− 9.9
	Mean loss 19.9 gm.		

* Dog that had a portacaval transposition with thrombosis of the anastomosis between the distal vena cava and the proximal portal vein.

weight of most of the dogs with a portacaval transposition was either sustained or slightly increased (Tables 3 and 4). The dogs with portacaval transposition also maintained normal activity and appetite, and none developed the syndrome of lassitude, anorexia, and polydipsia observed in the animals with Eck fistulas.

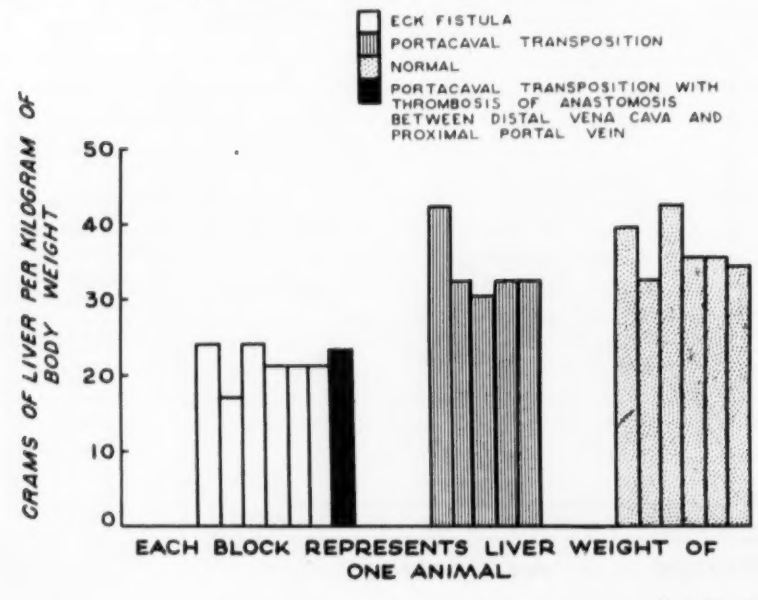
TABLE 4.—*Total Circulating Plasma Albumin, in Grams, in Dogs with Portacaval Transposition*

Dog No.	Preoperative	Three Mo. Postoperative	Net Change
138	43.8	83.5	+39.7
154	19.2	28.8	+ 9.6
113	50.2	38.8	−11.4
168	32.6	50.0	+17.4
	Mean gain 13.8 gm.		

The gross appearance of the livers was normal in both groups of animals except that the livers of the dogs with Eck fistulas were usually smaller. These findings are in agreement with those of Whipple, who described marked atrophy of the liver in dogs with Eck fistulas. On the other hand, as Figure 5 shows, the relation between the liver weights and the body weights in the dogs with portacaval transposition compared favorably with the normal.

Microscopic study of the livers of the animals with Eck fistulas revealed a tendency to the accumulation of fat in the central zones of the lobules and a loss of hepatic cells adjacent to the central vein. Figure 6 is a photomicrograph that is typical of the livers of the animals in this group. The glycogen content of the cells was also decreased. These changes were present in the livers of all of the dogs in Group 1, varying only in degree with respect to a given specimen. The livers of the dogs in Group 2 were entirely normal, and glycogen and fat were present in normal amounts. Figure 7 is a photomicro-

Fig. 5.—Comparison of the relation of liver weight to body weight in normal dogs, dogs with Eck fistulas, and dogs with portacaval transpositions.



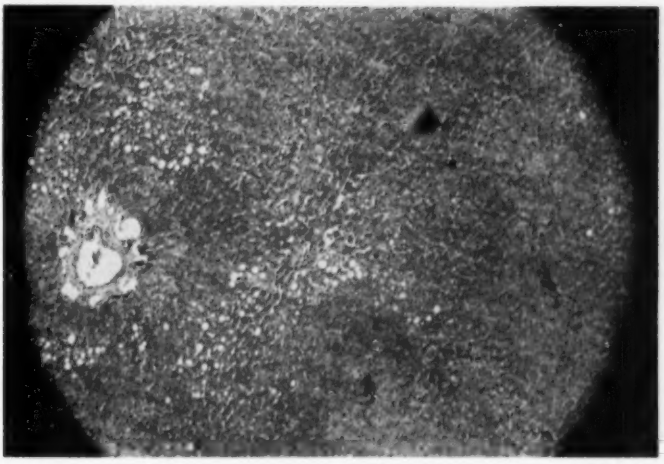


Fig. 6.—Histologic section of the liver of one of the animals with an Eck fistula.

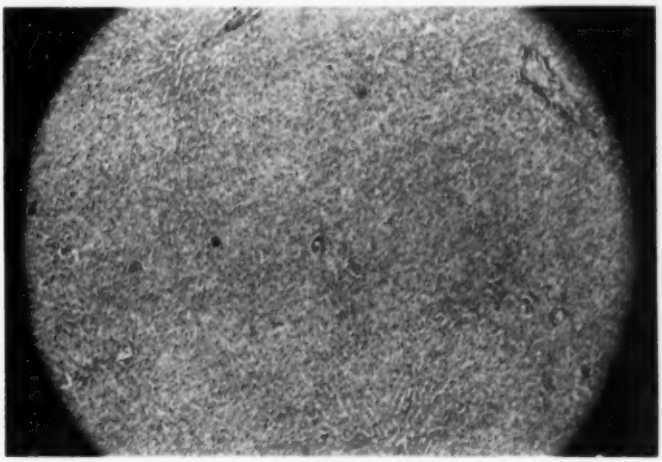
graph of the liver of one of the dogs in Group 2.

In one dog with a portacaval transposition the repair of a tear in the wall of the portal vein at the time of operation necessarily compromised the lumen of the anastomosis between the distal vena cava and the proximal portal vein. This anastomosis was found to be occluded at autopsy, although the other was still patent. As a result, in essence this animal had an Eck fistula with at least partial obstruction of the return of the venous blood from the kidneys and lower extremities, and in respect to liver function, clinical signs and symptoms, and relation of liver weight to its body weight, this dog reacted in a manner typical of the dogs with Eck fistulas, as described above.

Summary

One group of dogs was prepared with Eck fistulas and another group with transposition of the portal vein and vena cava. Sulfobromophthalein (Bromsulfalein) clear-

Fig. 7.—Histologic section of the liver of one of the animals with portacaval transposition



ance, tolerance to orally administered ammonium lactate, and thymol turbidity and serum protein determinations were made preoperatively and postoperatively.

The general condition of the dogs with Eck fistulas was poor; they lost weight, and there was a decrease in the total circulating plasma albumin. A gradual decline in sulfobromophthalein clearance also occurred. The fasting levels of ammonium nitrogen in the blood were found to be increased when measured three months following operation. In the dogs with Eck fistulas tolerance to orally administered ammonium lactate was considerably less than that of the normal animals or of those with portacaval transpositions. The livers of the animals with Eck fistulas were atrophic and showed evidence of fatty infiltration, decrease in glycogen content, and loss of cells in the central zones.

Both laboratory and histologic findings in the dogs with transposition of the portal vein and vena cava were very similar to those of normal animals. There was no significant loss of weight, and the total circulating albumin increased in every animal of the group except one. The clearance of sulfobromophthalein increased after the portacaval transposition operation. The livers and kidneys of these dogs were of normal weight, and there were no gross or microscopic abnormalities. The fat and glycogen contents of their livers were normal.

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REFERENCES

1. Whipple, G. H.; Robscheit-Robbins, F. S., and Hawkins, W. B.: Eck Fistula Liver Subnormal in Producing Hemoglobin and Plasma Proteins on Diets Rich in Liver and Iron, J. Exper. Med. 81:171, 1945.

2. Knutti, R. E.; Erickson, C. C.; Madden, S. C.; Rekers, P. E., and Whipple, G. H.: Liver Function and Blood Plasma Protein Formation: Normal and Eck Fistula Dogs, J. Exper. Med. 65:455, 1937.

3. Harper, H. A.; Gardner, R. E.; Johansen, R.; Galante, M., and McCorkle, H. J.: Amino Acid Tolerance in Experimental Portacaval Anastomosis, Surgery 29:210, 1951.

4. Ripstein, C. B.: Experiences with Portacaval Anastomosis in the Treatment of Portal Hypertension, Surgery 34:570, 1953.

5. Cohn, R.: A Skeptical Evaluation of Portacaval Anastomosis for Gastrointestinal Hemorrhage in Cirrhosis of the Liver, Stanford M. Bull. 9:231, 1951.

6. Mann, F. C., and Magath, T. B.: Production of Chronic Liver Insufficiency, Am. J. Physiol. 59:485, 1922.

7. Child, C. G., III; Barr, D. P.; Holswade, G. R., and Harrison, C. S.: Liver Regeneration Following Portacaval Transposition in Dogs, Ann. Surg. 138:600, 1953.

8. Wolfson, W. Q.; Cohn, C.; Calvary, E., and Ichiba, F.: Studies in Serum Proteins: V. A Rapid Procedure for the Estimation of Total Protein, True Albumin, Total Globulin, Alpha Globulin, Beta Globulin, and Gamma Globulin in 1.0 Ml. of Serum, Am. J. Clin. Path. 18:723, 1948.

9. Maclagan, N. F.: The Thymol Turbidity Test: New Indicator of Liver Dysfunction, Brit. J. Exper. Path. 25:234, 1944.

10. Mateer, J. G.; Baltz, J. I.; Steele, H. H.; Brouwer, S. W., and Colvert, J. R.: Chronic Subclinical Impairment of the Liver, J. A. M. A. 133: 909, 1947.

11. Goodman, R. D.: Bromsulfalein Clearance: A Quantitative Clinical Test of Liver Function, J. Lab. & Clin. Med. 40:531, 1952.

12. Gaebler, O. H.: Determination of Bromsulphalein in Normal, Turbid, Hemolyzed, or Icteric Serums, Am. J. Clin. Path. 15:452, 1945.

13. Conway, E. J.: Microdiffusion Analysis and Volumetric Error, New York, D. Van Nostrand Company, Inc., 1950.

14. Laws, J. F., and Everson, T. C.: Significance of Decreased Dye Clearance by the Liver Following Portacaval Anastomosis, J. Lab. & Clin. Med. 37:515, 1951.

DISCUSSION

ON PAPERS BY DRS. DYE, CAPPS, BAKER, GROVE, AND JULIAN AND DRS. SILEN, MAWDSLEY, AND HARPER

DR. ALFRED M. LARGE, Detroit: I should like to compliment both speakers on their contributions and excellent presentations and, if I may, discuss briefly both the experimental and the clinical aspects of this very important subject.

Experimentally, it seems to me, the work of Dr. Silen and his associates tends to indicate that it would be smart for us to continue to avoid complete portacaval shunts in our patients whenever we can.

Now, many of you will recall that some years ago there was presented from our laboratory experimental evidence to show that when animals were poisoned with carbon tetrachloride they tolerated shunting procedures much less well if complete Eck fistula was performed than if side-to-side portacaval anastomosis was done. We felt this to be at least indirect evidence in favor of splenorenal or side-to-side portacaval shunt. It seems to me that Dr. Silen's work is further evidence in favor of this concept.

About that time, several years ago, we thus thought it wise to do most of our shunts as side-to-side portacaval shunts, and we described a method which to us, at least, seemed easier technically than end-to-side portacaval shunt and which I think some of you have tried and, I hope, have found satisfactory. Surely it would appear to be a more physiological procedure not to divert all the portal blood away from the liver if this is technically feasible.

The difficulty, I think, with the splenorenal anastomosis is that, unless the spleen is very large, the vein too is small, and the shunt is then very likely to close, as Dr. Dye has pointed out.

With regard to the actual technique, which was so beautifully demonstrated in Dr. Dye's film, we have felt rather strongly that an everting type of suture is important, and those of our shunts that have closed and bled again, or that have been found closed at autopsy, have almost invariably been those performed with simple over-and-over stitch without eversion.

The other point that I should like to mention, if I may, is that I feel the emergency treatment of esophageal bleeders is still rather unsatisfactory. If the double balloon tube, described by Patton and our president (and by others), works in stopping the hemorrhage, that's all right; but in those cases in which it does not work, particularly those with cirrhosis, if one has to go in and do a transesophageal ligation, as has been described by Crile and Linton and others, one may surely stop the bleeding, but the patient has a nasty tendency to go into hepatic coma and die. Indeed, my feeling is so strong on this point that I now urge the performance of a prophylactic portacaval shunt in any persons who are found to have definite varices, even though they have not bled.

I think the over-all results in these shunt procedures are not very good, but surely shunts are the best thing we have available for the treatment of the patient with bleeding esophageal varices. When it is remembered that the mortality in these patients, which in the past has been perhaps 80% within a year, has now been pretty much reversed, so that 80% are now alive a year after operation, I am sure it is agreed that these operations are well worth continuing and perfecting more thoroughly.

Dr. Jacob K. Berman, Indianapolis: The splendid papers by Drs. Dye and Silen and their colleagues are stimulating, and again illustrate the importance of continual reappraisal of all forms of treatment as our experience increases.

I should like to ask Dr. Dye whether or not these patients had ascites, because that is a very important point. Almost 10 years have passed since we first advocated interdiction of the competition between arterial and portal venous inflow in the management of late and complicated atrophic cirrhosis of the liver. This we thought could be better accomplished by diminishing the arterial, rather than the portal venous, component.

The surgeon is asked to help when compensatory mechanisms have failed and complications, such as ascites and bleeding varices, ensue. Fortunately, in Groups I and II of our classification, where ascites is minimal and liver function not badly disrupted, medical management may be helpful, and often curative. However, in Group III, with bleeding varices, and Group IV, with a combination of uncontrolled ascites and bleeding esophageal varices, surgery is definitely indicated. These are the groups which are now under discussion.

One may attempt the permanent restraint of hemorrhage by direct means, which remove the bleeding zones, or by indirect measures, which seek to lower portal pressure. In the latter category the surgeon must decide whether he wishes to "arterialize" the liver, by completely or partially diverting portal venous flow, or to "portalize" the liver, by gradually diminishing the hepatic arterial flow.

Where bleeding varices alone are present (Group III), a portacaval shunt is helpful. The end-to-side is easier to perform but is perhaps less physiological than the introduction of additional shunts.

Patients with uncontrolled ascites or bleeding varices and ascites with poor hepatic function (Group IV) are those who are unsuitable for any surgical treatment except, perhaps, repeated paracenteses. Such patients are often helped by a gradual or leisurely occlusion of the hepatic artery close to the liver, with simultaneous ligation of the splenic and left gastric arteries. Our methods for accomplishing this have changed and cannot be described in the limited time allowed for this discussion.

Incidentally, our first two patients treated by hepatic, splenic, and left gastric arterial ligation about 10 years ago are still free from ascites and bleeding.

Dr. Egbert Howard Fell, Chicago: The history and findings in the case of a 7-year-old Hawaiian girl, cared for at the Presbyterian Hos-

pital in Chicago, emphasize a number of points made by the authors of the two papers.

In October, 1951, at the age of 4 years, the patient developed severe gastrointestinal hemorrhage. Roentgenograms revealed extensive esophageal varicosities. A diagnosis of cavernous thrombosis of the portal vein was made, and the patient was sent to a hospital in the United States, where a splenorenal shunt was successfully made. Following the shunt procedure, the splenic vein pressure was reduced from 400 to 200 mm. of isotonic saline pressure. The patient made an uneventful recovery from surgery and was well for three months. The esophagogram still showed extensive varicosities. In March, 1952, she had the first postoperative hemorrhage, which was repeated in November, 1953, and again in June, 1954. The severity of bleeding increased with each successive episode. The last bleeding could not be controlled, and the child was flown to Chicago.

The past history is irrelevant. The child was healthy and lived normally until the first hemorrhage.

On entrance to the hospital, the child was apathetic and pale and appeared very ill. Her blood pressure was 116/72; pulse, 138 a minute; temperature, 100 F (rectal), and respirations, 20 a minute. An intravenous needle was in the right saphenous vein. The previous left thoracoabdominal incision was well healed. There were no cutaneous varicosities, no ascites, and the liver was not palpable.

The laboratory findings on admission were as follows: hemoglobin, 4 gm. per 100 cc.; red blood cells, 1,320,000; white blood cells, 26,000; neutrophils, 8.8%; eosinophils, 1%; lymphocytes, 19%; monocytes, 2%. The blood chemistry and urine studies were within normal limits.

While being studied and prepared for surgery, the patient had a massive hemorrhage, which was controlled by a Sengstaken tube and blood replacement.

At surgery, on July 3, 1954, the portal area was exposed through a thoracoabdominal incision in the eighth right intercostal space. The diaphragm was partially incised. There were no dilated vessels or increased vascularity in the hepatic or gastrocolic omentum. The gastroesophageal junction was free of dilated veins. The liver appeared normal. The right kidney was enlarged as compared with the left, but both felt normal to palpation.

A normal-appearing portal vein, ½ in. in diameter, was dissected from the retroduodenal area to just beneath the porta hepatis. A single vein was seen to join the right-angle turn posteriorly and disappeared into the retroperitoneal tissue medial to the vena cava. At the convexity of the angulation a small fibrous band ascended into the liver at the porta hepatis. This appeared to be a rudimentary structure or a remnant of the portal vein. A pressure of 340 mm. of isotonic saline was present in the portal vein. The portal vein was sectioned at the most proximal point, and an end-to-side portacaval anastomosis was performed, using the everting type of suture. The fibrous band was ligated and divided. At the end of anastomosis, the portal pressure had dropped 60 to 280 mm. of isotonic saline pressure.

The postoperative course was uneventful, and there was no episode of bleeding. However, the child ran an unexplained fever, with temperatures up to 102 F at times. Because of this, the discharge date from the hospital was delayed to 23 days after surgery. All hematologic and bacteriologic studies to account for the fever remained uninformative. At the time of discharge the patient had no complaints and appeared well.

A liver biopsy specimen taken at surgery was considered normal histologically. Seventeen days after surgery the alkaline phosphatase, bilirubin, sulfobromophthalein clearance, and proteins all were within normal limits. A roentgenogram of the esophagus taken 23 days after surgery showed varices similar to those seen in the preoperative examination. X-ray studies nine months after surgery showed the varices to be greatly diminished throughout the length of the esophagus.

For two and a half years following surgery there has been no recurrence of bleeding, and the child is reported to be living normally.

DR. JOHN HARPER GRINDLAY, Rochester, Minn.: The story Dr. Silen told you about Eck fistula in the dog is a common experience for any one who has performed this procedure on a normal dog. However, if, on the other hand, the Eck fistula is made on a dog that has previously had a complete occlusion of its portal vein, it does not make any difference. He remains a perfectly normal dog. I do not know what it means, but apparently, if the liver is normal, and not cirrhotic, but suffers only from extrahepatic portal block, there is no deleterious effect. There is complete diversion of the portal blood into the vena cava.

I should like to make one remark about Dr. Dye's paper. It strikes me, if one were to look at these data impartially, that in the performance of the shunt on a patient with a cirrhotic liver his survival is a pretty good test that his liver was able to withstand the procedure.

DR. HAROLD LAUFMAN, Chicago: What Dr. Grindlay has just said appears also to be the case in the human being.

I notice in Dr. Blakemore's contribution in "Christopher's Textbook of Surgery," edited by Loyal Davis, that he states flatly he now prefers the end-to-side anastomosis of the portal vein

and the vena cava. Since his patients do so well (and certainly he has a large experience), it would seem that in the cirrhotic patient, like the cirrhotic dog, the end-to-side anastomosis seems to be satisfactory. I suspect the reason is that there are many collateral portal channels into the liver substance in such a cirrhotic patient. Experiments on noncirrhotic dogs, therefore, may not be directly applicable.

DR. WILLIAM S. DYE, Chicago: We also have had extremely poor results with emergency surgery in bleeding varices, having had four patients out of six die. Death was due to hepatic coma.

One must admit, however, that we operated on these patients in a more terminal stage than Dr. Linton has recommended. We have not performed any prophylactic shunts. In regard to ascites, there is no way of predicting whether a shunt will help or not.

Dr. Grindlay's point about the patient withstanding a procedure such as portacaval shunt is certainly well taken.

We have ascribed to Dr. Laufman's point, in that we feel that many of these patients already have complete obstruction and diversion of the portal flow, a situation which is not the same as that of a patient with a normal liver.

Extrapleural Posterolateral Approach for Upper Thoracic Sympathectomy

A Preliminary Report

ROBERT T. CROWLEY, M.D., Williamson, W. Va., and DONALD E. ECONOMY, Detroit

At the present time several operative approaches are advocated for removing the upper thoracic sympathetic ganglia in treatment of vasospastic diseases of the upper extremity, such as Raynaud's disease. Adson and Brown [1] removed the upper thoracic sympathetic ganglia through a paraspinal, extrapleural approach. Palumbo [3] approached the ganglia through an anterior transpleural incision, and Crandell and Bosien [2] initiated the transaxillary, transpleural approach.

In the dorsal approach of Adson and Brown [1] exposure is accomplished by incision and retraction of the heavy musculature between the scapula and the spine, with removal of one or more of the transverse processes in the upper thoracic area. This procedure presents the following disadvantages:

1. Respiration during anesthesia is markedly handicapped with the patient in the face-down position.

2. The necessity of removing the transverse process to expose the ganglia adequately may, in its removal, distort or destroy existing anatomic sympathetic relationships.

3. Improper identification of the second or third rib may inadvertently place the operator too high on the sympathetic chain, and an accidental removal of the stellate ganglion would result, with a Horner syndrome as its sequela.

4. If an inadequate amount of sympathetic chain is removed inferiorly, because of inadequate exposure, an incomplete denervation of the upper extremities, with persistence of the patient's symptoms, would result.

In the transthoracic approach of Palumbos',[3] where the exposure and localization of the sympathetic component is effected by an anterior thoracotomy incision, the localization of the sympathetic chain is most adequate. However, the patient is thereby prone to all the complications of an intrapleural procedure, namely, failure of lung reexpansion, pulmonary trauma, and empyema.

In the transaxillary approach, the localization and excision of the appropriate sympathetic segments are carried out by a high axillary intercostal incision directly into the pleural cavity. The excision of the selected sympathetic structure is readily effected, but, because the pleural space is entered, there is an increased hazard of pulmonary complications. Additionally, the axillary incision traverses vital structures in this area, which may be traumatized.

It is the purpose of this report to describe a method successfully employed by us in which segmental excision of the upper thoracic sympathetic ganglia and intervening trunk can be readily accomplished. This technique presents the following advantages:

1. It offers adequate exposure, minimal blood loss, and correct identification of the

Read at the 64th Annual Meeting of the Western Surgical Association, Cincinnati, Dec. 1, 1956.

From the Departments of Surgery of Wayne State University College of Medicine, Detroit, Detroit Receiving Hospital, and Veterans Administration Hospital, Dearborn, Mich., and the Department of Surgery, Memorial Medical Center, Williamson, W. Va.

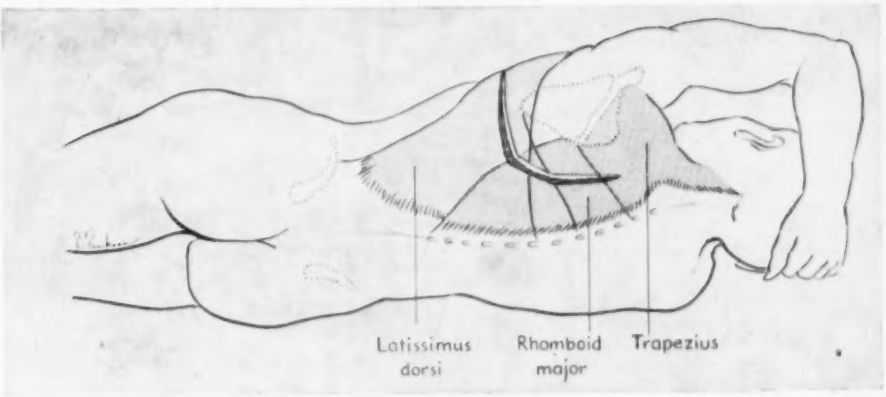


Fig. 1.—Position of patient and localization of the skin incision.

sympathetic ganglia by proper identification of the overlying third rib.

2. The pleural cavity is not entered, thereby avoiding possible complications attendant thereto.

3. Deformity is minimal.

4. The procedure itself is simply a limited modification of a procedure already familiar to many, namely, that of thoracoplasty.

As practiced by us, the technique is carried out as follows: With the endotracheal anesthesia, with the patient in the conventional recumbent position, and after the proper surface preparation, a circumscapular incision, similar to that employed for thoracoplasty, is made. This incision extends from the level of the scapular spine, posteromedially, to the anterior axillary line, anterolaterally. The trapezius, rhomboideus, and latissimus dorsi muscles are divided, as in a conventional thoracotomy incision, and the scapula is elevated (Fig. 1).

A count of the ribs from above downward is performed, and the fifth rib is identified. The upper margin of this rib is stripped of its soft tissue over a sufficient area in its posterior third to allow the insertion and secure maintenance of one flange of a Finochietto retractor. The other flanged end of the retractor is placed beneath the angle of the scapula, and the retractor is adjusted to allow full and ready access to the upper ribs by separation of the scapula from the posterolateral chest wall. The third rib and its transverse process are identified, and a segment of that rib is stripped of its periosteum and removed for a distance of approximately 3 in., extending from the transverse process anteriorly (Fig. 2).

The periosteal bed of the third rib is then incised along its entire exposed area, and the intact pleura is carefully dissected by blunt manipulation with the examining finger away from the posterior chest wall toward the spine. As this dissection proceeds posteriorly, the sympathetic trunk and ganglia are readily identified lying just medial to the transverse processes and along the posterolateral aspects of the bodies of the vertebrae. The sympathetic ganglia of the second, third, and fourth thoracic segments, their intervening chain, and their intercostal nerve rami communicantes are easily identified. The interruption of the sympathetic chain is then accomplished in the usual manner by elevation of the proper structures into the incision. We transect the sympathetic chain between the third and fourth ganglia, sever the rami communicantes of the second and third intercostal nerves, and then suture the proximal sympathetic chain to the intercostal muscles in the area, to prevent future regeneration of the chain (Fig. 3).

After this manipulation, hemorrhage, if present, is easily controlled. The wound is closed in layers without drainage and an

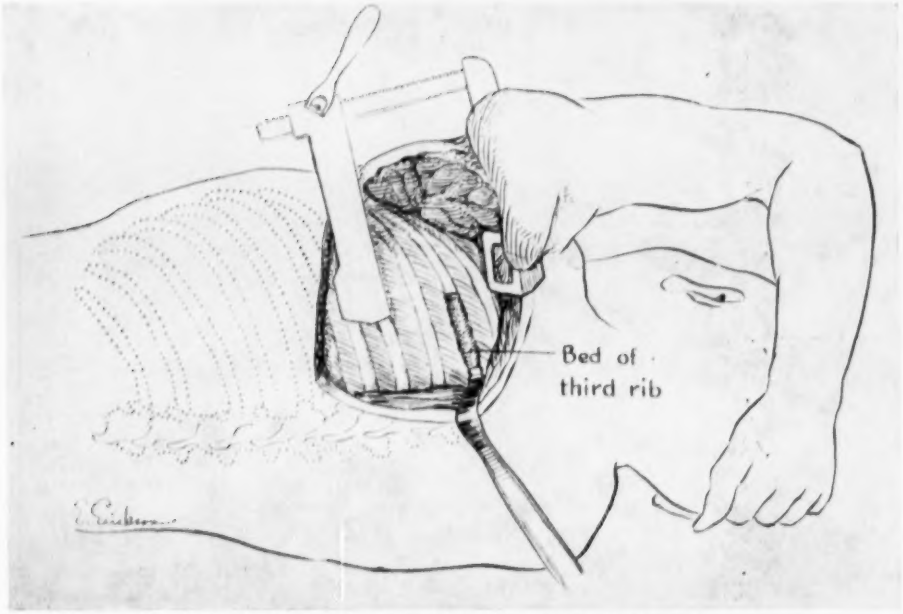
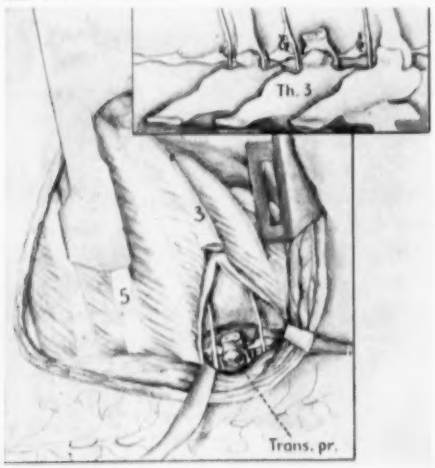


Fig. 2.—Exposure of the third rib with scapula elevated.

appropriate dressing applied. Fine cotton or silk suture is used throughout. It is perhaps appropriate to emphasize that the transverse process and the head of the rib need not be removed for exposure, and that if exposure or excision is difficult, an additional segment of the second or fourth rib can be removed to facilitate excision. This has not been necessary in any of our cases. Furthermore, any thoracotomy or thoracoplasty procedure previously performed in the operative area does not contraindicate or materially impede the use of this technique, in spite of the existence of pleural thickening or chest wall scarring, if some additional care is taken.

Fig. 3.—Exposure of upper thoracic sympathetic chain after a segment of the third rib has been resected.



The one disadvantage to the above-described technique is cosmetic. A sufficiently long circumscapular incision must be made to allow adequate displacement of the scapula, in order better to expose the upper five ribs and their transverse processes. Such an incision naturally results in the familiar long, parascapular external scar, without change in contour of the thoracic cage. However, where the cosmetic consideration can be disregarded, this procedure is extremely satisfactory.

Our five cases were unattended by any pulmonary, cardiac, or ocular complications. Pain in the recovery phase was minimal, and convalescence was uneventful. By resecting the second and third thoracic ganglia, we

completely denervated the sympathetic supply to the upper extremity and the anterior and posterior chest wall down to the fourth intercostal space, as evidenced by anhidrosis of these areas.

Summary

Selective excision of the upper segments of the thoracic sympathetic chain is frequently employed for the relief of various vasospastic disorders of the upper extremity.

Several procedures are described and utilized to accomplish such excision, each possessing certain inherent disadvantages.

An additional technique to accomplish this purpose is described, and its advantages and disadvantages are indicated.

Memorial Medical Center.

DISCUSSION

DR. HIRAM THOMAS LANGSTON, Chicago: In this era, when the impetus seems to be to open more and more body cavities simultaneously, it is indeed refreshing to come back to the advocation of a conservative approach. Now, I presume that those who are not used to the old days of doing thoracoplasty might consider this incision rather gruesome and large, but it must be pointed out that for adequate exposure of the upper ribs in the thoracic cage a general exposure is necessary, in order to mobilize the scapula.

Dr. Crowley's point concerning the necessity for the larger incision is a good one, because if you use the limited approach, you will be working in a deep well through the back muscles and, therefore, the visibility and the exposure are far less satisfactory. The extension upward for an inch or two of this incision will give you much more exposure than the extension downward.

I do not care to discuss the adequacy of the sympathetic chain resection. That is a point beyond my depth. The approach, however, is one of interest, and I do feel warmly about the conservatism, rather than the extension toward radicalism.

DR. WILLIAM H. POTTER, Harlan, Ky.: As a Yankee who has moved to Kentucky, devoid of actual experience with this particular incision for this purpose, it is pleasantly inappropriate that I should be asked to comment before the Western Surgical Association. In spite of having been taught to feel it sinful to be caught talking about operative technique, I'm grateful for the opportunity to indulge in a little sin.

We find the clinical result to be better if the pathologist reports nerve in the specimen of sympathectomy tissue sent to the laboratory. As Gordon Madding has said, "If you can see it, you can do it." This, of course, helps us to avoid profanity, loss of adrenaline, and loss of sleep consequent to uncontrolled bleeding in the depths of a hole.

If we get too concerned with cosmetic results in the Smithwick or any of the neurosurgical posterior buttonhole approaches, we find ourselves soul-searching for principles underlying surgical exposure. There is an insidious propaganda of the plastic surgeons which, in the interest of the patient, we must be careful to suppress into the limit of its true perspective. We must repeat, "Wounds heal from side to side and not from end to end."

If one's incision requires use of a head mirror, a spotlight headband gadget, laryngeal mirrors, and tools over 10 in. long, that is tantamount to confession that the exposure is not all that could be desired.

As a matter of convenience, the more surgery we can do with standard instruments, the better. Whenever we find it necessary to introduce special tools into a procedure we advocate for general use, we introduce additional hazards to the patient because we make it complicated.

Henry Head, for this reason, has preferred the use of the main part of a Balfour retractor to the Finochietto retractor to spread ribs. A technique that is adapted to our standard general surgery instruments is preferable in that it is likely to serve more patients by remaining within the province of the general surgeon.

I am glad to see that the authors use endotracheal anesthesia. I have found that every time I start bragging about an extrapleural approach, into the pleura I go. Then I have to decide whether to drain.

To those familiar with thorascoplasty, Dr. Crowley's incision will give the pleasant feeling, not of exploring uncharted territory, but of coming back home.

REFERENCES

1. Adson, A. W., and Brown, G. E.: Treatment of Raynaud's Disease by Resection of the Upper Thoracic and Lumbar Sympathetic Ganglia and Trunks, Surg. Gynec. & Obst. 48:577, 1929.

2. Crandell, W. B., and Bosien, W. R.: Transaxillary Approach for Upper Thoracic Sympathetic Ganglionectomy, Ann. Surg. 142:28, 1955.

3. Palumbo, L. T.: Anterior Transthoracic Approach for Upper Thoracic Sympathectomy, A. M. A. Arch. Surg. 72:659, 1956.

4. Atkins, H. J. B.: Peraxillary Approach to the Stellate and Upper Thoracic Sympathetic Ganglia, Lancet 2:1152, 1949.

Surgery Illustrated

End-to-Side Portacaval Shunt

JOHN L. MADDEN, M.D., New York

Comment

End-to-Side Portacaval Shunt

Arthur B. Blakemore, M.D., and Arthur B. Voorhees Jr., M.D., New York

The key to a successful portacaval shunt is a rapidly moving stream of blood. The precise mechanism by which the process of thrombosis is accelerated in a slow-moving stream or retarded in a fast-moving stream is not known, but for practical purposes this observation may be accepted for fact. A high rate of flow can be achieved where the pressure within the portal system is high and the pressure within the vena cava or renal vein is low, thereby establishing a satisfactory pressure gradient. A high rate of flow can be further assured by minimizing peripheral resistance, particularly in the portal or the splenic vein. Angulation and constriction of the vein along its course or at the site of anastomosis, or turbulence in the vena cava or renal vein in close proximity to the stoma of the shunt, may spell disaster. In the gradual evolution of the portacaval shunt as a surgical procedure, we hold the foregoing facts in a position of paramount importance in the planning and execution of the operation.

(*Comment continued on page 980*)

PLATE I

A, the patient is placed in the supine position and the right side is elevated to an angle of 40 to 45 degrees from the horizontal. The thoracoabdominal incision overlying the ninth intercostal space is in dotted outline.

B, C, D, the incision is deepened through the subjacent musculature, the costal arch, the diaphragm, the pleura, and the peritoneum to expose the underlying intraperitoneal and intrapleural viscera.

E, the liver is displaced downward and then rotated and retracted upward into the adjacent right pleural cavity. The hepatic flexure of the colon is mobilized by severance of the right phrenocolic ligament as indicated in dotted outline.

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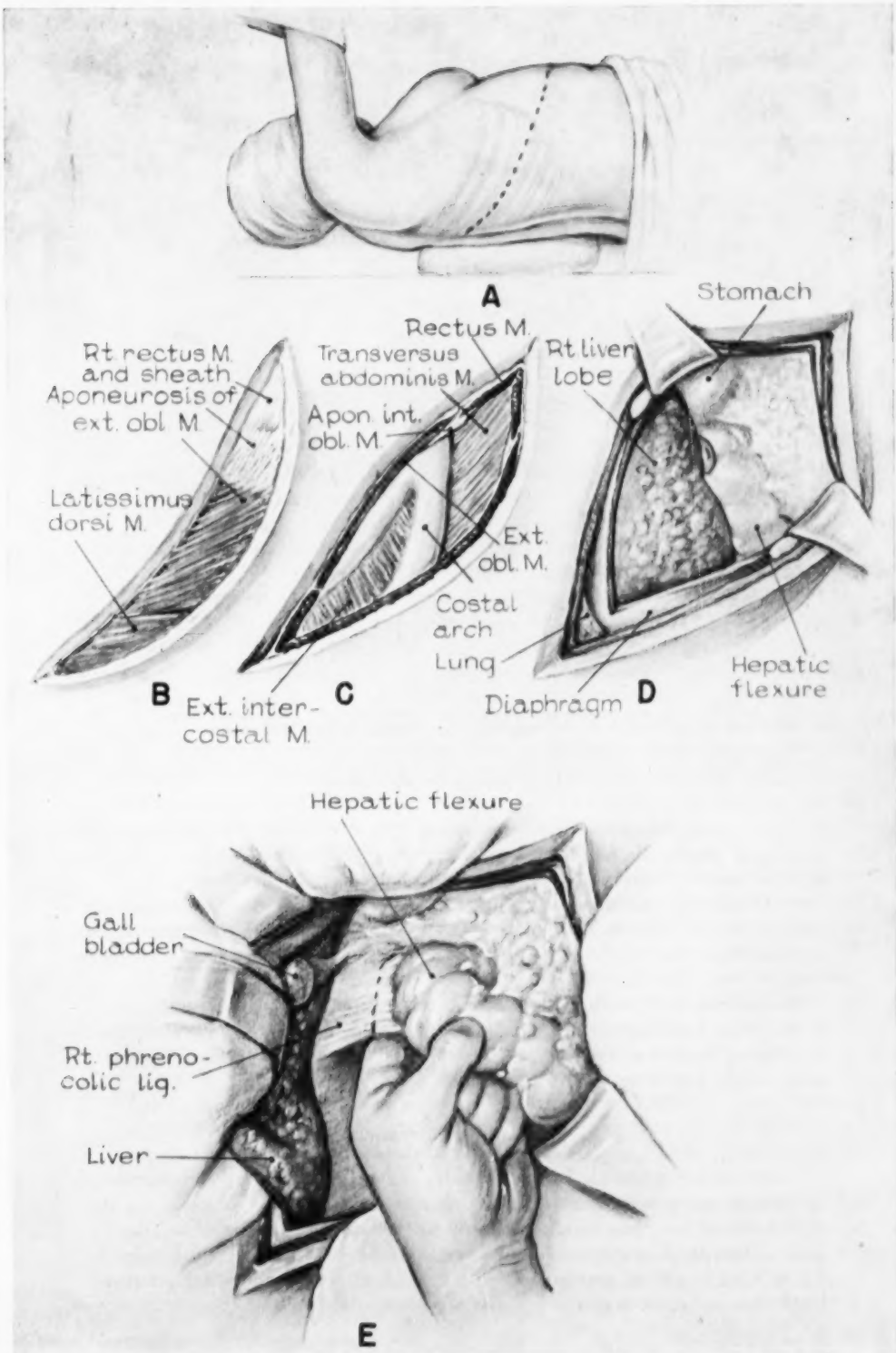
This article is the last of four based on "Atlas of Technics in Surgery," by Dr. Madden, to be published in September, 1957, by Appleton-Century-Crofts, New York.

Department of Surgery, St. Clare's Hospital, 415 W. 51st St. (19) (Dr. Madden).


A
Rt rectus M. and sheath
Aponeurosis of ext. obl. M.
Latissimus dorsi M.
B
Rectus M.
Transversus abdominis M.
Apon. int. obl. M.
Ext. obl. M.
Costal arch
Ext. inter-costal M.
C
Stomach
Rt liver lobe
Lung
Diaphragm
D
Hepatic flexure
Hepatic flexure
Gall bladder
Rt. phreno-colic lig.
Liver
E

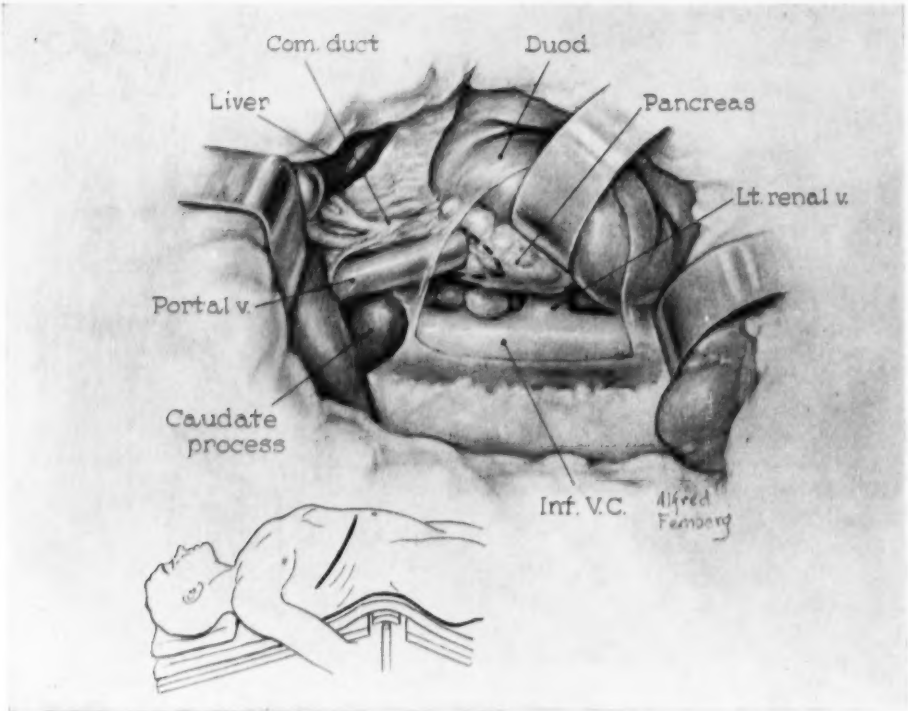


Fig. 1.—The first and second portions of the duodenum have been rotated medially. The anterior and medial aspects of the vena cava have been exposed. The relation of the portal vein, common duct, and caudate process to one another is outlined. The dotted line represents the usual wedge of pancreatic tissue that is resected to prevent angulation and compression of the portal vein when it is shifted into position for the anastomosis.

As a result of animal experimentation and observation derived from 350 portacaval shunts in the human, we are convinced that the end-to-side portal-vein-to-vena-cava anastomosis is the most efficient and that the side-to-side portal-vein-to-vena-cava anastomosis and the end-to-side splenic-vein-to-renal-vein anastomosis are less efficient. These differences in efficiency are reflections of the rates of flow that can be usually achieved by the three major shunt configurations.

In addition to these broad considerations, scrupulous attention must be paid to the gentle handling of the veins and to the maintenance of aseptic conditions. A crushing forceps or insignificant infection may represent the initial nidus of a subsequently occluding thrombus.

General Considerations

Strict aseptic technique in the operating room is imperative. In addition to the usually accepted methods of skin sterilization and sterile draping, the use of helmets rather than caps, double masks rather than single masks, double-glove technique during the skin incision, and skin towels carefully applied by Michel's clips spaced approximately 2 cm. apart serve two useful functions. First, this technique minimizes possible contamination of the operative site by

bacteria from the skin, nasal and oral pharynx, and the hair. Second, if one insists on such a technique, which is somewhat at variance from the routine, the operating room personnel is constantly alerted to the need for extraordinary precautions. As a further precaution, 300,000 units of fortified procaine penicillin and 1 gm. of streptomycin are administered intramuscularly to the patient immediately prior to the skin incision. This will provide an adequate therapeutic level of antibiotics within the body during the course of the operative procedure.

The Technique of Portal-Vein-to-Vena-Cava Shunt

The patient is placed in a supine position on the operating table so that the break in the table or kidney elevator is at the approximate level of the third lumbar vertebra (Fig. 1). A flat sandbag is then placed under the right shoulder, and another similar sandbag is placed under the right hip. Side-braces suitably padded are placed along the left lateral chest wall and at the level of the left hip, thereby permitting subsequent tilting of the table to the left approximately 15 degrees. The right arm can either be suspended from the ether screen or allowed to rest at the patient's side. By breaking the table and elevating the kidney elevator, the patient is placed in a hyperextended position. After careful skin preparation and sterile draping, the skin incision is made for the thoracoabdominal approach. The line of incision commences at the anterior anxillary line over the ninth rib and is carried obliquely, medially across the costal margin to a point approximately 2-3 cm. above the umbilicus in the midline of the abdomen. The skin incision is deepened through the subcutaneous tissue to the level of the deep fascia, and at this point skin towels are applied with the use of Michel's clips spaced approximately 2 cm. apart. The incision is then deepened through the muscle layers to the level of the periosteum of the ninth rib. The periosteum is stripped from the ninth rib, and the rib is transected at the midaxillary line. The rib and its costal cartilage are then resected. Medially, the incision is deepened through the oblique musculature, anterior and posterior rectus sheaths, and peritoneum. After entry into the peritoneal cavity, the remainder of the thoracic portion of the incision is completed by entering the chest cavity through the bed of the ninth rib, incising the diaphragmatic pleura and peritoneum, and splitting the diaphragm in the course of its muscle fibers for approximately 12-15 cm. After general abdominal examination and confirmation of the diagnosis, a specimen for biopsy is obtained from the right lobe of the liver by making a cruciate incision through the liver capsule on the anterior margin and inserting a cork borer, of approximately 5 mm. in diameter, to the depth of 4 cm. The plug of liver tissue thus obtained is immediately given to the pathologist for early fixation. Bleeding from the biopsy site is controlled by suitably placed mattress sutures tied over a plug of skeletal muscle.

For the sake of convenience, the subsequent operative procedure can be divided into three parts. The first step is that of mobilization of the duodenum and identification and partial mobilization of the inferior vena cava. The second step is identification and mobilization of the portal vein. The third step is the anastomosis of the portal vein to the vena cava.

Step 1 (Fig. 1).—The peritoneal reflection overlying the first and the second portion of the duodenum is incised along the greater curvature of the first and second portions of the duodenum. By blunt and sharp dissection, the first and second portions of the duodenum are rolled toward the midline. When the

(Comment continued on page 984)

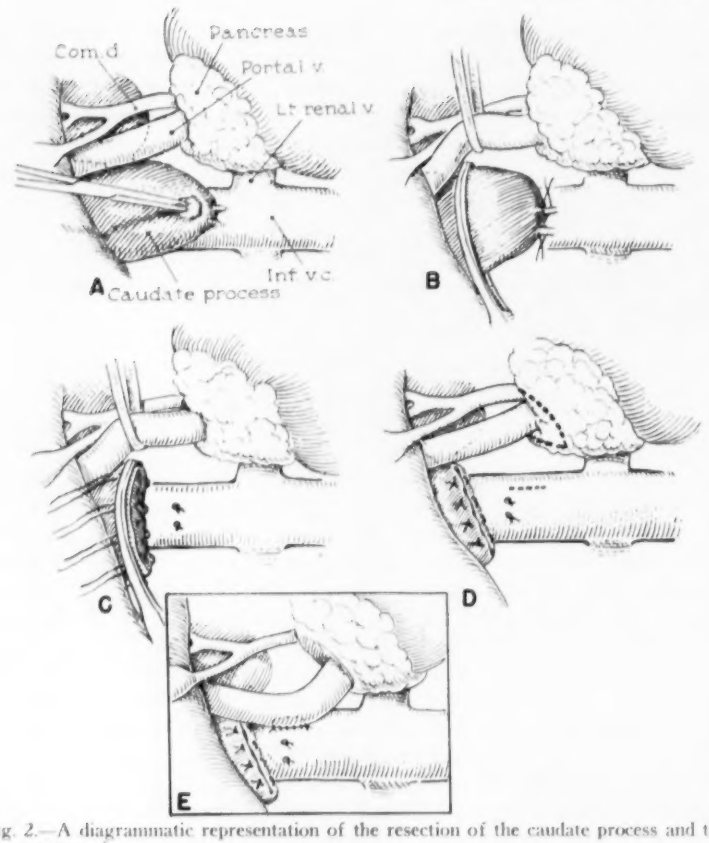


Fig. 2.—A diagrammatic representation of the resection of the caudate process and the side-to-side anastomosis.

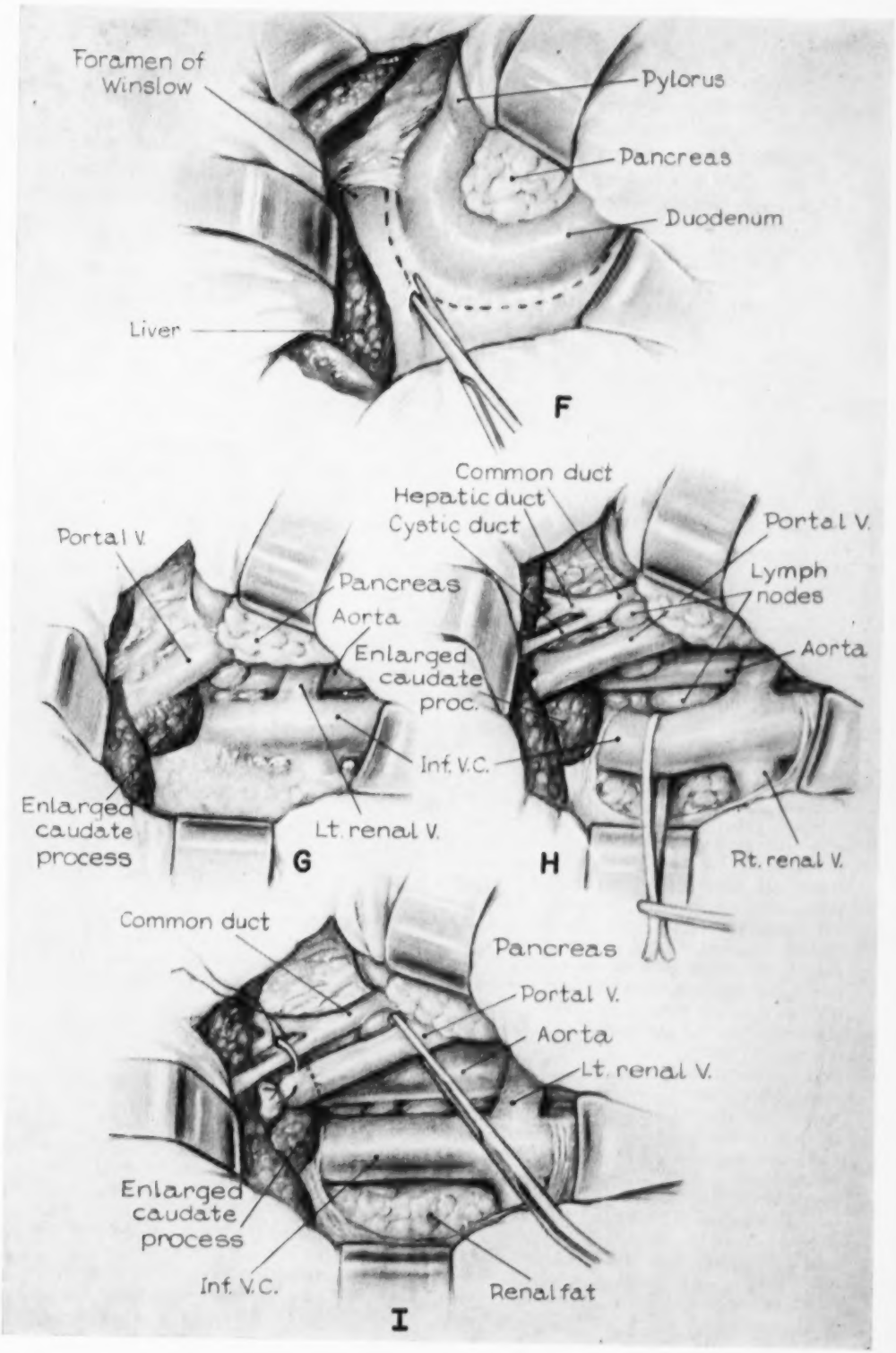
PLATE II

F, the mobilized hepatic flexure of the colon is displaced downward toward the left lower quadrant of the peritoneal cavity, and the foramen of Winslow, the pylorus, the head of the pancreas, and the retrocolic portion of the duodenum are exposed. Mobilization of the descending portion of the duodenum is commenced by scissor dissection of the posterior parietal peritoneal layer along its lateral border (Kocher maneuver). Normally, this peritoneal layer, like the posterior layer of the lienorenal ligament, is avascular and may be severed with impunity. However, in the presence of portal hypertension the application of clamps to prevent excessive blood loss may be required.

G, the mobilized segment of the duodenum and the head of the pancreas are retracted toward the midline to expose the related structures as depicted.

H, the dissection is continued, and the structures are now more clearly visualized. The dissection and isolation of the structures shown is both tedious and difficult because of the edema and increased vascularity of the tissues. The mobilized segment of the inferior vena cava is encircled by a traction tape of rubber tissue and partially retracted to expose clearly the group of lymph nodes between the aorta and the inferior vena cava.

I, the proximal portion of the portal vein is occluded, first proximally with an angulated Potts' ductus clamp, and then distally with a ligature and a suture ligature of silk (00) respectively. The site for transection of the portal vein is indicated in dotted outline. The convergence cephalad of the portal vein and the inferior vena cava and their separation by the caudate process of the liver may be readily seen. In some instances partial resection of an enlarged caudate process, as suggested by Blakemore, may be required to permit the performance of a portacaval shunt.


Foramen of Winslow
Pylorus
Pancreas
Duodenum
Liver
F
Common duct
Hepatic duct
Cystic duct
Portal V.
Portal V.
Lymph nodes
Pancreas
Aorta
Aorta
Enlarged caudate proc.
Inf. V.C.
Enlarged caudate process
Lt. renal V.
G
H
Rt. renal V.
Common duct
Pancreas
Portal V.
Aorta
Lt. renal V.
Enlarged caudate process
Inf. V.C.
Renal fat
I

undersurface of the pancreas can be identified along the lesser curvature of the duodenum, the medial mobilization of the duodenum has been sufficient. With the duodenum in its medial reflected position, the vena cava lies immediately posterior to the area from which the second portion of the duodenum was reflected. The overlying strands of areolar tissue can be divided with safety along the anterior midline of the vena cava. If the right spermatic or ovarian vein is visible, the anterior mobilization of the vena cava has been begun too far caudad. For the purposes of the operation, it is usually sufficient to mobilize only the anterior and medial aspects of the vena cava from the level of the left renal vein to the caudate isthmus of the liver. Mobilizing the right lateral aspect of the vena cava in this region is unnecessary and extremely hazardous because of the numerous veins coming from the adrenal gland and entering the vena cava directly. It is also important to identify with precision the left renal vein, since it will subsequently represent a landmark in selection of the site of anastomosis. In certain patients hypertrophy of the caudate process may encroach upon the subsequent site of anastomosis, and in these instances the caudate process must be resected (Fig. 2). When this is the case, it is necessary to ligate two or more pairs of minute veins running from the caudate process to the vena cava. These are frequently unrecognized during manipulation of the process and may be torn, giving rise to troublesome hemorrhage in an area difficult to control. Once the caudate process has been freed from the underlying vena cava, it can be cross clamped and resected. Hemostasis is achieved by multiple vertical mattress sutures placed approximately 1 cm. from the cut margins.

Step 2.—It must be remembered that with the patient in a hyperextended left semilateral position the operator is usually looking at the right lateral aspect

(*Comment continued on page 986*)

PLATE III

J, the whole of the circumference of the inferior vena cava superior to the renal veins is completely mobilized, and its lumen is partially occluded by a Potts-Smith clamp. However, if desired, a Potts' curved portacaval clamp may be used. The advantage of this type of clamp is that a longitudinal segment of the inferior vena cava may be occluded without the necessity of mobilizing the whole of the circumference of the inferior vena cava. The proximal transected end of the portal vein is turned downward toward the inferior vena cava preliminary to the performance of the veno-venal shunt. The dotted line in the occluded segment of the inferior vena cava indicates the site of the incision for the anastomosis.

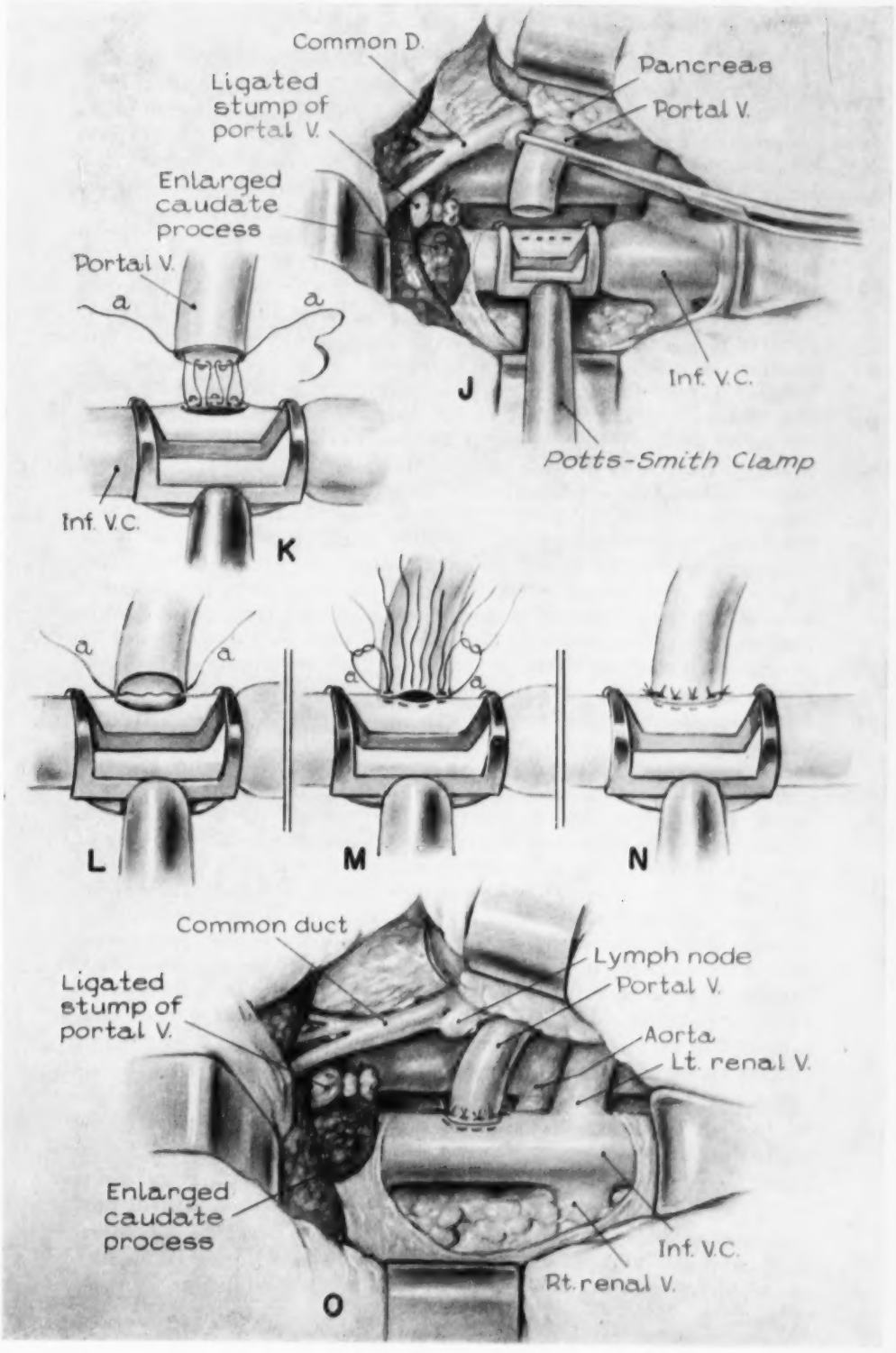
K, the posterior suture layer of the anastomosis is inserted. This is a continuous eversion type of suture (silk, 00000) with intima-to-intima approximation. The suture is commenced from the "outside-in" on the portal vein and terminates from the "inside-out," also on the portal vein. In between its commencement and termination the suture proceeds from the "inside-out" to the "outside-in" relative to the lumen of the portal vein and the inferior vena cava. Accordingly, the "loops" formed by the suture are always on the outside of the lumen of the vessels.

L, the posterior suture, *a-a*, is drawn taut, and the intimal surfaces of the portal vein and vena cava are in close approximation. None of the silk suture is exposed within the lumen.

M, a series of interrupted everting mattress sutures of silk (00000) is employed for the anterior layer of the anastomosis. All these sutures are first inserted and then tied. The mattress sutures at either end are tied first and one of the long ends of each of these sutures is in turn tied to either end, *a-a*, of the continuous everting suture of silk used for the posterior layer.

N, the intervening mattress sutures are tied to complete the anterior layer of the anastomosis.

O, the operative field upon completion of the end-to-side portacaval shunt is shown.


Common D.
Pancreas
Ligated stump of portal V.
Portal V.
Enlarged caudate process
Portal V.
a
a
J
Inf. V.C.
Potts-Smith Clamp
Inf. V.C.
K
a
a
a
a
L
M
N
Common duct
Lymph node
Portal V.
Ligated stump of portal V.
Aorta
Lt. renal V.
Enlarged caudate process
Inf. V.C.
Rt. renal V.
O

of the hepatoduodenal ligament, and in this position the common duct lies in an anterior location and the portal vein in a posterior location in the ligament (Fig. 1). The peritoneal investment of the hepatoduodenal ligament is incised in the posterior right lateral aspect of the hepatoduodenal ligament from the porta hepatis to the greater curvature of the duodenum. In making this incision, care should be exercised to avoid cutting unnecessarily any recognizable lymphatic channels. Once the peritoneum is incised, the vein can usually be identified by finger dissection and palpation. Upon identification, the vein should be dissected bluntly in the adventitial plane at roughly its midportion between the porta hepatis and the head of the pancreas. Following local circumferential dissection of the vein, a short piece of umbilical tape can be passed about the vein for the purposes of gentle traction. This serves as a useful method for avoiding unnecessary instrumentation of a vein subsequently to be used as a shunt. The dissection is carried cephalad to the porta hepatis. The bifurcation of the portal vein into the right and left hepatic veins should be identified. This represents the highest point of dissection, and at this time there are usually no significant venous tributaries which must be dealt with. The portal vein is mobilized caudad by sharp and blunt dissection of the level of the head of the pancreas. Two major tributaries to the portal vein, if unrecognized, may tear and cause troublesome hemorrhage. The first tributary is on the medial aspect of the portal vein and enters directly into the head of the pancreas. The second tributary is on the lateral inferior aspect of the portal vein, just beneath a collar of pancreatic tissue where the portal vein emerges from the head of the pancreas. Both tributaries should be identified and individually ligated by transfixation ligatures of 00000 braided silk. After mobilization of the portal vein, it is appropriate to make initial pressure readings in the portal system from a large branch of the gastroepiploic vein. Simple manometric readings, using the manubrial notch as the reference point, should be made with the portal vein open and then with the portal vein compressed. If the pressure rise following compression of the portal vein is in excess of 150 mm. of saline, then a side-to-side, portal-vein-to-vena-cava anastomosis is advised. As the last portion of this second step in preparation for an end-to-side anastomosis, a ligature of heavy silk is passed about the portal vein at the level of the bifurcation into the right and left hepatic veins. The ligature is tied, and a second transfixion suture employing 00 braided silk is placed approximately 3 mm. from the primary tie. A rubber-shod clamp that will occlude, but not crush, the vein is placed around the vein as it emerges from the head of the pancreas, and the vein is transected immediately proximal to the transfixion suture. Twenty to thirty cubic centimeters of a solution of heparin containing 10 mg. of heparin in 100 cc. of saline is instilled in the portal vein proximal to the rubbershod clamp.

Step 3.—An imaginary line coursing parallel to the vena cava on its anterior medial aspect, equidistant from the true anterior aspect of the vena cava and the true left lateral aspect of the vena cava, which may be identified by the juncture of the left renal vein, is defined and marked by two arterial silk sutures as the future axis of the anastomosis (Fig. 3). The vena cava is tended and grasped by a Beck-Potts clamp. An oval window is then cut in the vena cava, corresponding in diameter to the fully distended portal vein. The anastomosis is placed as near to the liver as practical so that the angle formed between the portal vein and the vena cava will be an acute angle, 45-60 degrees. A single

layer anastomosis is achieved by a simple over and over suture of 00000 braided silk. It is desirable to exert some tension on the angle stay sutures during the anastomosis to avoid purse stringing the stoma. In the posterior suture line care must be exercised to avoid dragging small strands of adventitial tissue into the suture line by the suture material. After completion of the anastomosis, the vena cava clamp is released first, and the portal vein clamp released second. Anastomoses in a low pressure system rarely leak seriously, and minimal suture line leaks occurring shortly after the removal of the clamps should be controlled by simple finger pressure over the area. Unless the suture line leak is a serious one, reenforcing sutures should not be taken, since they may cause distortion or constriction of the stoma. Once flow has been established in the newly formed shunt, the point of emergence of the portal vein from the region of the head of the pancreas should be carefully examined. Frequently a collar of pancreatic tissue will cause angulation or actual compression of the portal vein in its newly established course. If this collar exists, a wedge of pancreatic tissue should be excised (Fig. 4). This compression feature is an exceedingly important one and may not be recognized by a cursory examination; it must be actively looked for.

In those instances where side-to-side anastomosis between the portal vein and the vena cava are deemed advisable because of a pressure rise in the portal system in excess of 150 mm. of saline following compression of the portal

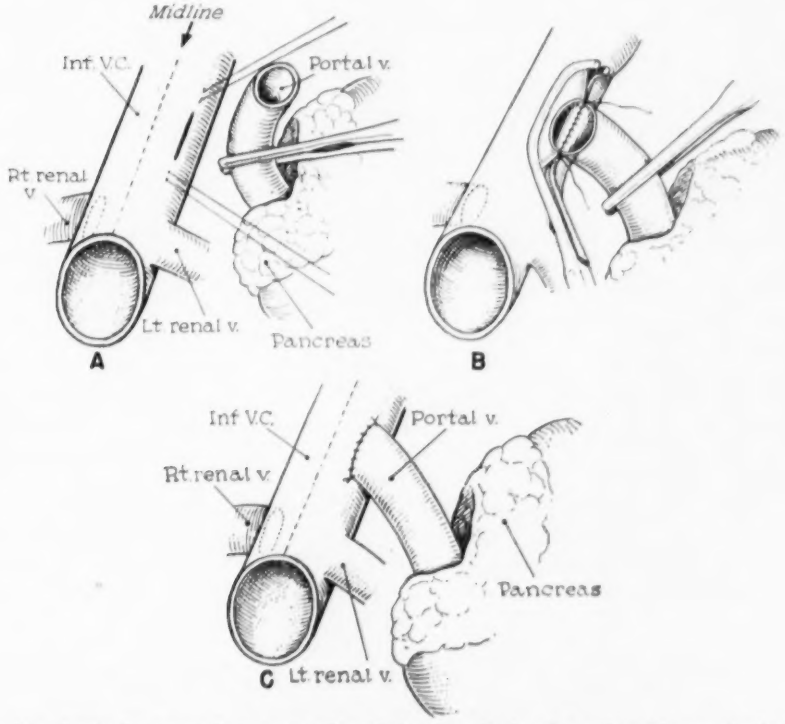


Fig. 3.—A diagrammatic representation of the site selection for end-to-side portal vein-to-vena cava anastomosis.

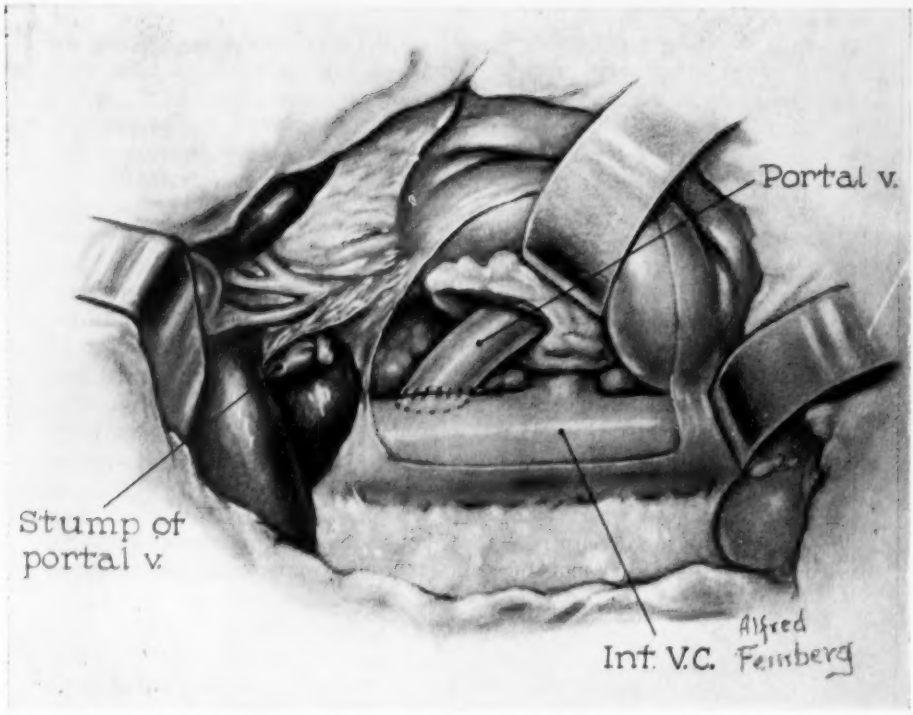
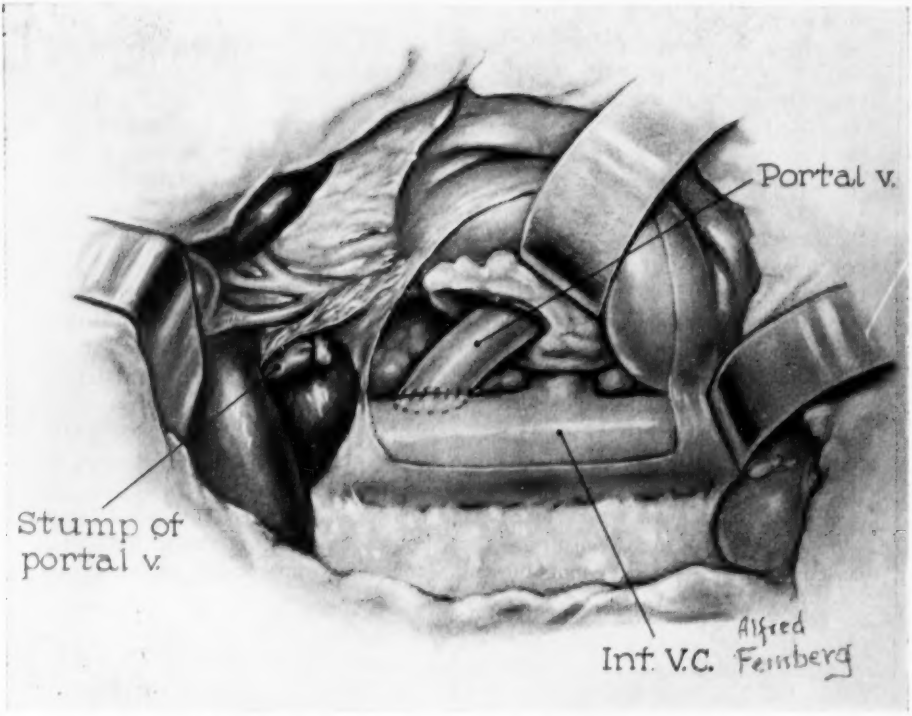


Fig. 4.—Artist's portrayal of the completed end-to-side portal vein-to-vena cava anastomosis, emphasizing the obliquity of the shunt and the wedge resection of the adjacent pancreas.

vein, the portal vein is not divided. Contiguous surfaces of the vena cava and portal vein are marked by arterial sutures, the vena cava is grasped by a Beck-Potts clamp in a fashion similar to that previously described, and a 15 mm. diameter oval window is cut (Fig. 2). The portal vein is temporarily occluded above and below the site of anastomosis by a simple double turn of unbilical tape, and a corresponding 15 mm. diameter oval window is cut in the previously marked site. The anastomosis is accomplished in precisely the same manner as that described for the end-to-side anastomosis.

After completion of the portal-vein-to-vena-cava shunt, manometric pressures are again recorded in the portal system, with and without portal vein compression. In ideal circumstances, the pressure in the portal system should be less than 200 mm. of water pressure. If this pressure has not been achieved, the possibility of mechanical impedance to flow by distortion of the portal vein, or at the site of anastomosis, should be excluded by inspection. In the closure of the operative wound no attempt is made at reperitonization or closing the retroperitoneal tissues over the site of anastomosis. The abdominal and thoracic portions of the wound are anatomically reconstituted. The abdomen is closed without drainage, and the chest cavity is closed over a large-caliber catheter, which is withdrawn at the conclusion of the chest closure after residual air and fluid have been evacuated from the cavity.

THE INDEX TO THIS VOLUME HAS BEEN REMOVED FROM THIS POSITION AND PLACED AT THE BEGINNING OF THE FILM FOR THE CONVENIENCE OF READERS



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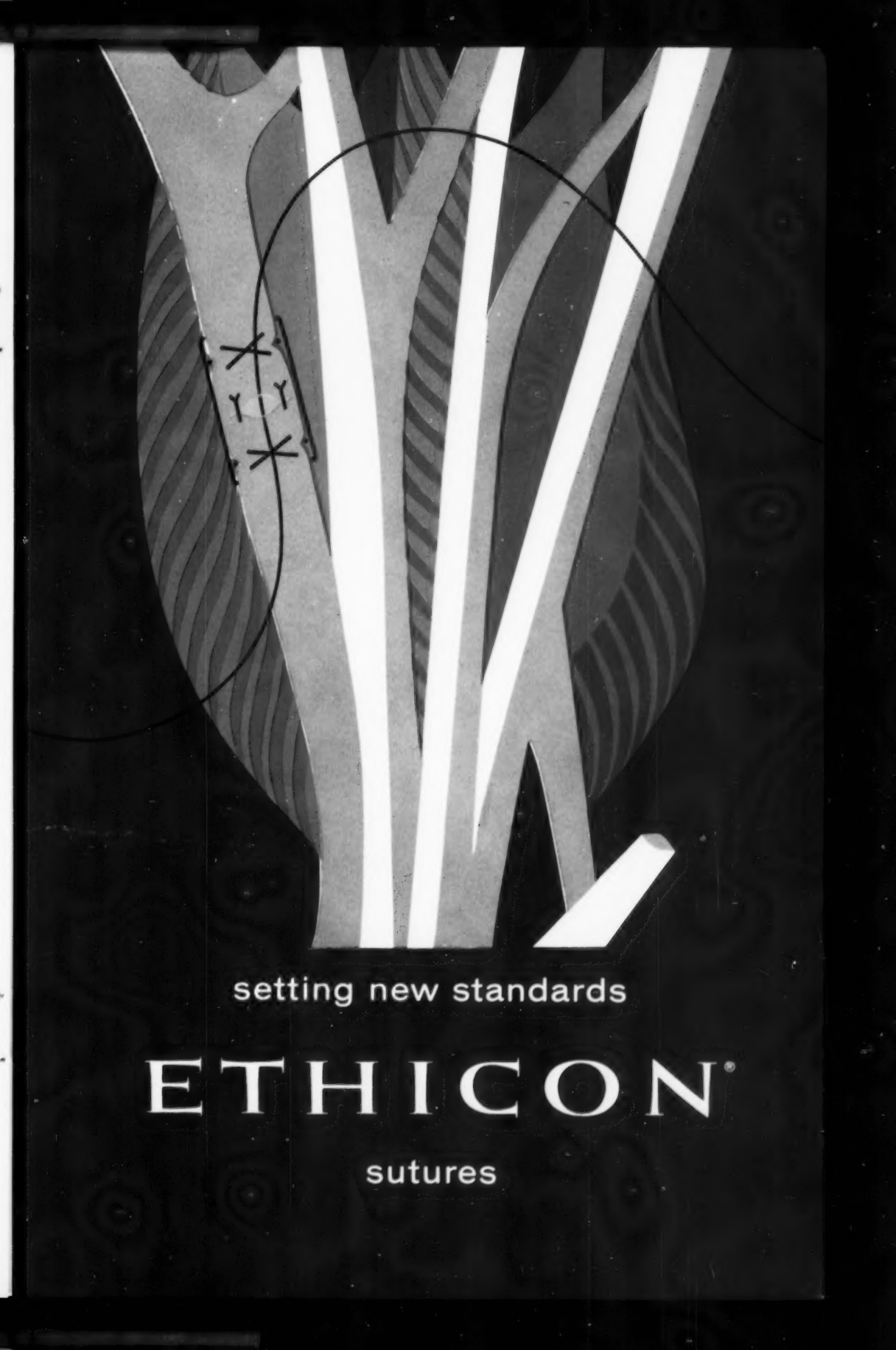
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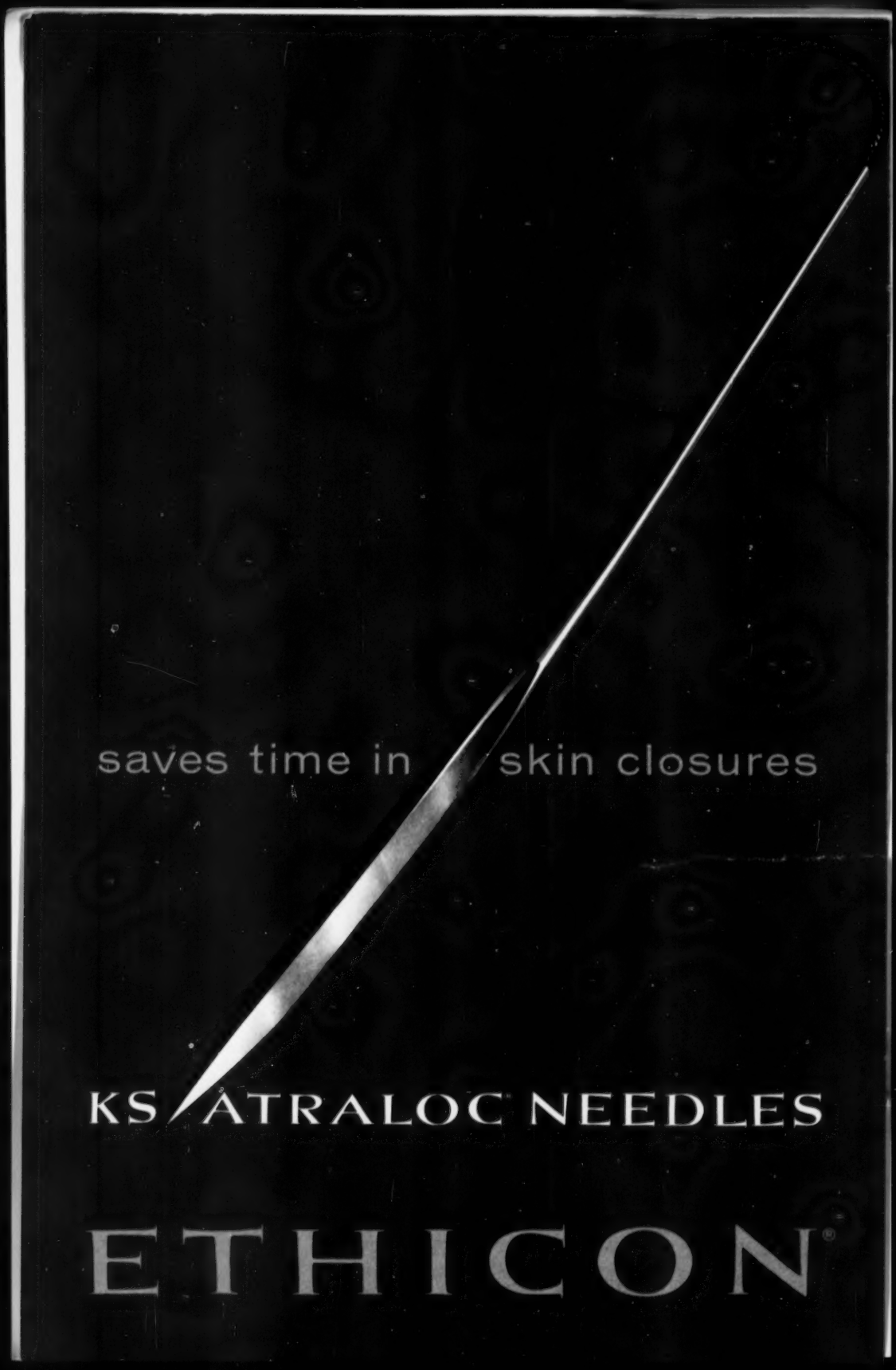
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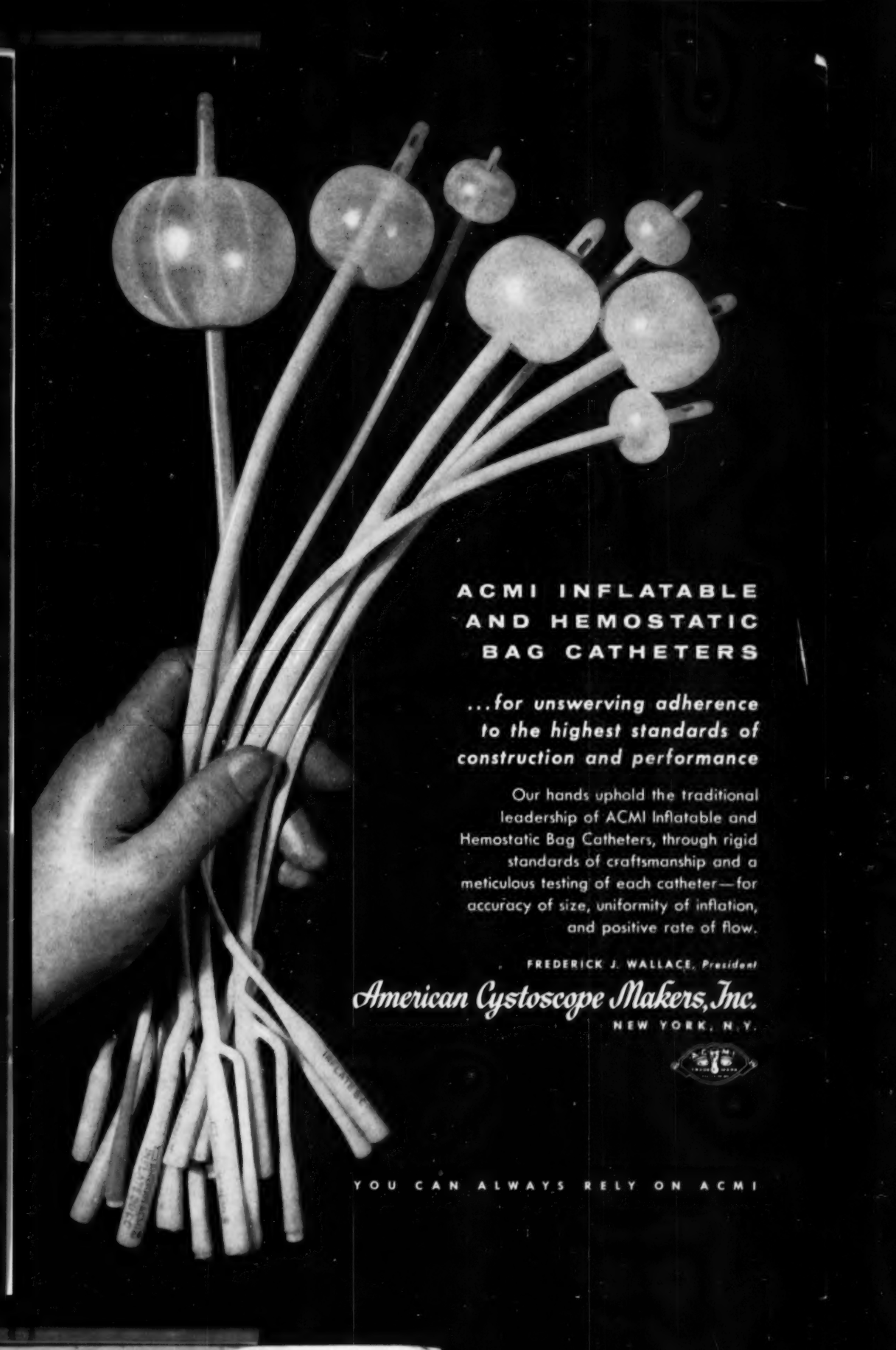

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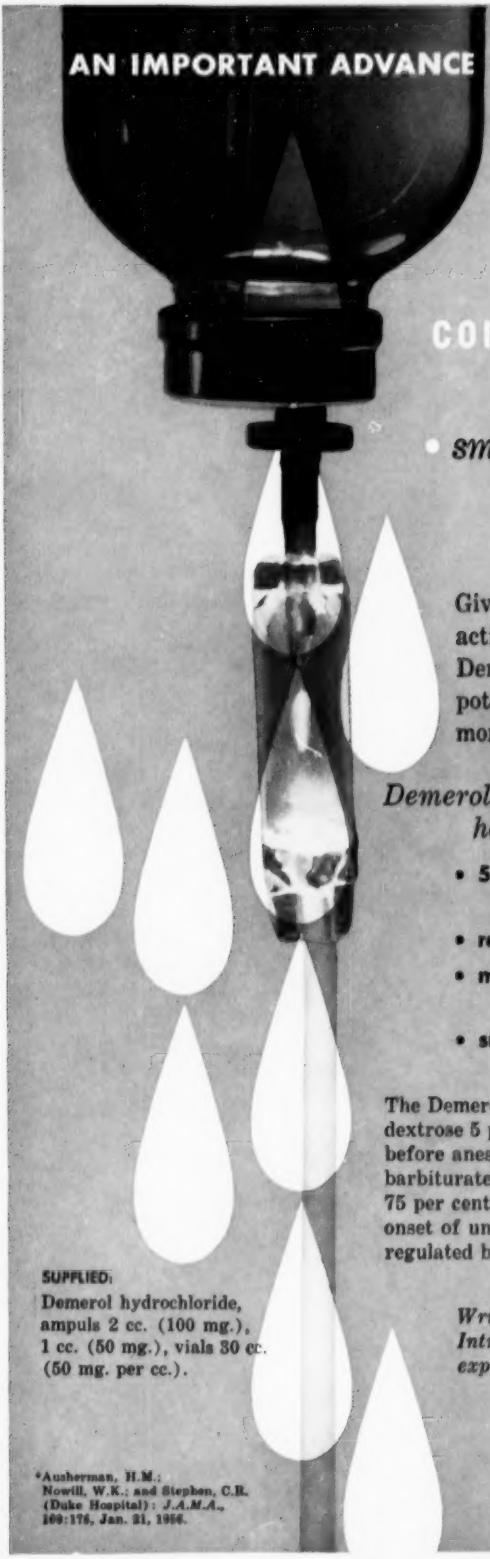

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*Ausherman, H.M.; Nowill, W.K.; and Stephen, C.R. (Duke Hospital): *J.A.M.A.*, 169:178, Jan. 31, 1959.

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